Thomas R. Curtin
George C. Jones
McElroy, Deutsch, Mulvaney & Carpenter, LLP
1300 Mount Kemble Ave.
P.O. Box 2075
Morristown, NJ 07962-2075
Tel: (973) 993-8100
Fax: (973) 425-0161

Attorneys for Defendant
Bionpharma Inc.

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

AZURITY PHARMACEUTICALS, INC.,	)	
	)	
Plaintiff,	)	C.A. No. 21-12870-MAS-DEA
	)	
v.	)	
	)	
	)	
BIONPHARMA INC.,	)	**(Public Version)**
	)	
Defendant	)	

DECLARATION OF R. CHRISTIAN MORETON, Ph.D.

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I, R. Christian Moreton, Ph.D., submit this declaration in support of Defendant Bionpharma Inc.'s ("Bionpharma") opposition to Plaintiff Azurity Pharmaceuticals, Inc.'s ("Azurity") motion for an order to show cause for temporary restraining order, preliminary injunction, and other emergent relief (ECF No. 25) ("Azurity's Motion"), and hereby declare as follows:

I. INTRODUCTION

1. I am a pharmaceutical formulator. I have been retained by Bionpharma as an expert in this case. I previously served as an expert on behalf of Bionpharma in connection with the following related actions: *Silvergate Pharmaceuticals, Inc. v. Bionpharma Inc.*, C.A. No. 18-1962-LPS (D. Del.) and *Silvergate Pharmaceuticals, Inc. v. Bionpharma Inc.*, C.A. No. 19-1067-LPS (D. Del.) (together, "the First Wave Suits"); and *Silvergate Pharmaceuticals, Inc. v. Bionpharma Inc.*, C.A. No. 20-1256-LPS (D. Del.) ("Second Wave Suit").

2. The First Wave Suits originally involved claims Azurity (as successor-in-interest to the original plaintiff in those suits, Silvergate Pharmaceuticals, Inc. ("Silvergate")) brought against Bionpharma alleging that Bionpharma's Abbreviated New Drug Application ("ANDA") No. 212408 ("Bionpharma's ANDA") seeking approval for a 1 mg/mL enalapril maleate oral solution product ("Bionpharma's ANDA product") infringes certain claims of U.S. Patent Nos. 9,669,008 B1 ("'008 patent") (ECF No. 9-3, July 13, 2021 Decl. of Roshan P. Shrestha, Ph.D. ("Shrestha Decl.") Ex. C), 9,808,442 ("'442 patent") (ECF No. 9-4, Shrestha Decl. Ex. D), 10,039,745 B2 ("'745 patent") (ECF No. 9-5, Shrestha Decl. Ex. E), and 10,154,987 B2 ("'987 patent") (ECF No. 9-6, Shrestha Decl. Ex. F), (collectively, "the First Wave Patents"). In response, Bionpharma raised defenses and counterclaims in the First Wave Suits contending that Bionpharma's ANDA and ANDA product do not and will not infringe the First Wave Patents. In connection with the First Wave Suits, I served on behalf of Bionpharma a Rebuttal Expert Report

("First Wave Rebuttal Report"). I also testified on behalf of Bionpharma at trial in the First Wave Suits. My testimony from trial in the First Wave Suits is attached hereto at Exhibits A (D. Del. 18-1962 ECF No. 195, Trial Tr. Vol. B) and B (D. Del. 18-1962 ECF No. 196, Sealed Trial Tr. Vol. B).

3. I have been advised by Bionpharma's counsel that, on April 27, 2021, the Delaware court presiding over the First Wave Suits rendered an opinion finding that Azurity failed to prove that Bionpharma's ANDA and ANDA product infringe the asserted claims of the First Wave Patents—including because Azurity failed to prove the existence of a buffer in Bionpharma's ANDA product—and, on April 20, 2021, entered final judgment of non-infringement in Bionpharma's favor.

4. The Second Wave Suit involved claims Azurity brought against Bionpharma alleging that that Bionpharma's ANDA and ANDA product infringe certain claims of U.S. Patent Nos. 10,772,868 B2 ("'868 patent") (ECF No. 9-11, Shrestha Decl. Ex. K), 10,786,482 B2 ("'482 patent"), (ECF No. 9-12, Shrestha Decl. Ex. L), and 10,918,621 B2 ("'621 patent") (ECF No. 9-13, Shrestha Decl. Ex. M) (collectively, "Second Wave Patents"). The Second Wave Patents claim priority to, and are within the same patent family as, the First Wave Patents. In response to Azurity's claims of infringement of the Second Wave Patents, Bionpharma raised various defenses and counterclaims contending that the asserted claims of the Second Wave Patents were invalid and that Bionpharma's ANDA and ANDA product would not infringe any asserted claims of the Second Wave Patents.

5. Because all of the claims of the Second Wave Patents require a buffer to maintain stability of the enalapril liquids claimed therein, I have been advised from Bionpharma's counsel that Bionpharma maintained that the Delaware's court's decision in the First Wave Suits rendered

moot Azurity's infringement claims in the Second Wave Suit. As such, I have been advised that the parties thereafter stipulated to dismissal of the Second Wave Suit, and that the dismissal was "with prejudice" (meaning, I have been advised, that Azurity cannot assert the same cause of action against Bionpharma again) absent a ruling on appeal in the First Wave Suits that would eliminate the Delaware court's rulings that rendered the Second Wave Suit moot.

6. Prior to the dismissal of the Second Wave Suit, I understand that Azurity had moved the Delaware court presiding over the Second Wave Suit for an order preliminarily enjoining Bionpharma from launching its ANDA product prior to a final disposition of the Second Wave Suit. It is my understanding that Bionpharma opposed Azurity's preliminary injunction motion, and, in support of that opposition, I prepared and executed a Declaration dated April 19, 2021, attached hereto as Exhibit C ("April 19, 2021 Moreton Declaration" or "my April 19, 2021 Declaration"). In my April 19, 2021 Declaration, I opined on the meaning of certain terms of the Second Wave Patents, and that Bionpharma's ANDA and ANDA product did not infringe certain claims of the Second Wave Patents, and that all claims of the Second Wave Patents were invalid. *See generally*, Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. My First Wave Rebuttal Report is attached as Exhibit A to my April 19, 2021 Declaration (Ex. C).

7. I have been further advised by Bionpharma's counsel that, on June 22, 2021, Azurity instituted the instant Third Wave Suit asserting that Bionpharma's ANDA and ANDA product infringe U.S. Patent No. 11,040,023 B2 ("'023 patent" or "patent-in-suit"). The '023 patent claims priority to, and is in the same family with, the First and Second Wave Patents. In response to the instant Third Wave Suit, I understand that Bionpharma has raised, or intends to raise, a number of defenses, including claim preclusion and invalidity defenses.

8. In the instant Declaration, I provide my preliminary opinions on the meaning of certain terms used in the claims of the '023 patent, and on Bionpharma's claim preclusion and invalidity defenses to those claims. I also opine on the non-infringement of claims 17 and 18 of the '023 patent. My Declaration also serves to rebut the opinions expressed in the Declaration of Declaration of Dr. Graham Buckton (ECF No. 25-6).

9. I hereinafter refer to Azurity's First Wave Patents, Second Wave Patents, and the '023 patent collectively as "Azurity's enalapril liquid patent family."

10. In preparing this Declaration, I have relied on my knowledge, training and experience, and the documents cited herein.

II. QUALIFICATIONS

11. My qualifications are set forth in paragraphs 7-16 of my First Wave Rebuttal Report (Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. Ex. A), and at page 374, line 5, through page 383, line 13, of my First Wave Suits Public Testimony (Ex. A, 18-1962 ECF No. 195, Trial Tr. Vol. B), and are incorporated as if fully set forth herein.

III. THE FIRST WAVE PATENTS

12. At paragraphs 22-66 of my First Wave Rebuttal Report (Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. Ex. A), I provided some general opinions on the First Wave Patents, including: (1) what certain claims of the First Wave Patents were directed to; (2) what was disclosed in the common specification of Azurity's enalapril liquid patent family;[1] and (3) the prosecution history of the First Wave Patents. I hereby incorporate those opinions as if fully set forth herein.

[1] Each patent in Azurity's enalapril liquid patent family contains essentially the same specification, which I herein refer to as "the common specification."

IV. THE SECOND WAVE PATENTS

13. At paragraphs 6-41 of my April 19, 2021 Declaration (Ex. C), I provided some general opinions on the Second Wave Patents, including: (1) what certain claims of the Second Wave Patents were directed to; (2) what was disclosed in the common specification of Azurity's enalapril liquid patent family; and (3) the prosecution history of the Second Wave Patents. I hereby incorporate those opinions as if fully set forth herein.

V. THE '023 PATENT

A. General Information

14. The '023 patent, entitled "ENALAPRIL FORMULATIONS," is directed to oral enalapril liquid formulations. ECF No. 1-1, Compl. Ex. A, '023 patent at Abstract. The '023 patent issued on June 22, 2021, from U.S. Patent Application No. 17/150,587, which was filed on January 15, 2021 ("'587 application"), and claims priority to U.S. Patent Application No. 16/991,575, filed on August 12, 2020 ("'575 application" (now the '621 patent)), which is a continuation of U.S. Patent Application No. 16/883,553, filed on May 26, 2020 ("'553 application"), which is a continuation of U.S. Patent Application No. 16/242,898, filed on January 8, 2019 ("'898 application" (now the '868 patent)), which is a continuation of U.S. Patent Application No. 16/177,159, filed on October 31, 2018 ("'159 application" (now the '482 patent)), which is a continuation of U.S. Patent Application No. 16/003,994, filed on June 8, 2018 ("'994 application" (now the '987 patent)), which is a continuation of U.S. Patent Application No. 15/802,341, filed on November 2, 2017 ("'341 application" (now the '745 patent)), which is a continuation of U.S. Patent Application No. 15/613,622, filed on June 5, 2017 ("'622 application" (now the '442 patent)), which is a continuation of U.S. Patent Application No. 15/081,603, filed on March 25, 2016 ("'603 application" (now the '008 patent)), and further claims priority to U.S. Patent Provisional Application No. 62/310,198, filed on March 18, 2016 ("'198 application").

ECF No. 1-1, Compl. Ex. A, '023 patent at cover. The '023 patent identifies Gerold L. Mosher and David W. Miles as the inventors and is assigned on its face to Silvergate. *Id*.

B. The Common Specification

15. As I have stated, above, the '023 patent shares a common specification with the First and Second Wave Patents. I have provided a general summary of the common specification at paragraph 27-39 of my First Wave Rebuttal Report (Exhibit A to Exhibit C hereto), and also at page 501, line 12, through page 509, line 15, and page 537, line 15, through page 538, line 22, of my First Wave Suits Sealed Testimony (Ex. B, D. Del. 18-1962 ECF No. 196, Sealed Trial Tr. Vol. B). Those opinions are hereby incorporated by reference as if fully set forth herein.

C. The Asserted Claims of the '023 Patent

16. The claims of the '023 patent recite as follows:

> 1. A stable oral liquid formulation, consisting essentially of: (i) about 0.6 to about 1.2 mg/ml enalapril or a pharmaceutically acceptable salt or solvate thereof; (ii) a sweetener; (iii) a preservative, wherein the preservative comprises sodium benzoate, a paraben or a mixture of parabens; (iv) water; and (v) optionally a flavoring agent; wherein the formulation is stable at about 5±3 °C. for at least 12 months; and wherein the stable oral liquid formulation has about 95% w/w or greater of the initial enalapril amount and about 5% w/w or less total impurity or related substances at the end of the given storage period.
>
> 2. The stable oral liquid formulation of claim 1, wherein the formulation is stable at about 5±3 °C. for at least 18 months.
>
> 3. The stable oral liquid formulation of claim 1, wherein the formulation is stable at about 5±3 °C. for at least 24 months.
>
> 4. The stable oral liquid formulation of claim 1, wherein the formulation maintains a pH between about 3 and about 4 for at least 3 months at about 5±3 °C.
>
> 5. The stable oral liquid formulation of claim 1, wherein the formulation maintains a pH between about 3 and about 4 for at least 12 months at about 5±3 °C.
>
> 6. The stable oral liquid formulation of claim 1, wherein the sweetener is sucralose.

7. The stable oral liquid formulation of claim 6, wherein the sucralose is present in about 0.5 mg/ml to about 0.9 mg/ml in the oral liquid formulation.

8. The stable oral liquid formulation of claim 1, wherein the sweetener is saccharin or a salt thereof.

9. The stable oral liquid formulation of claim 8, wherein the saccharin or a salt thereof is present at about 2 mg/ml in the oral liquid formulation.

10. The stable oral liquid formulation of claim 1, comprising a flavoring agent.

11. The stable oral liquid formulation of claim 1, wherein the enalapril or a pharmaceutically acceptable salt or solvate thereof functions as a buffer.

12. The stable oral liquid formulation of claim 1, wherein the enalapril or a pharmaceutically acceptable salt or solvate thereof is present at about 1.0 mg/ml in the oral liquid formulation.

13. The stable oral liquid formulation of claim 1, wherein the preservative is a mixture of parabens.

14. The stable oral liquid formulation of claim 1, wherein the paraben or the mixture of parabens is methylparaben, ethylparaben, propylparaben, butylparaben, salts thereof, or a combination thereof.

15. The stable oral liquid formulation of claim 1, wherein the mixture of parabens comprises methylparaben and propylparaben.

16. The stable oral liquid formulation of claim 1, wherein the paraben or the mixture of parabens is present at about 0.1 mg/ml to about 2 mg/ml in the oral liquid formulation.

17. The stable oral liquid formulation of claim 1, wherein the preservative comprises sodium benzoate.

18. The stable oral liquid formulation of claim 17, wherein the sodium benzoate is present at about 0.2 mg/ml to about 1.2 mg/ml in the oral liquid formulation.

19. The stable oral liquid formulation of claim 1, consisting essentially of: (i) about 1.0 mg/ml enalapril or a pharmaceutically acceptable salt or solvate thereof; (ii) a sweetener that is sucralose or sodium saccharin; (iii) a preservative, wherein the preservative comprises a mixture of parabens that is present at about 0.1 mg/ml to about 2 mg/ml in the oral liquid formulation; (iv) water; and (v) optionally a flavoring agent.

20. The stable oral liquid formulation of claim 1, consisting essentially of: (i) about 1.0 mg/ml enalapril or a pharmaceutically acceptable salt or solvate thereof; (ii) a sweetener that is sucralose or sodium saccharin; (iii) a

> preservative, wherein the preservative comprises sodium benzoate that is present at about 0.2 mg/ml to about 1.2 mg/ml in the oral liquid formulation; (iv) water; and (v) optionally a flavoring agent.

ECF No. 1-1, Compl. Ex. A, '023 patent at claims.

D. The Prosecution History of the '023 Patent

17. The '587 application was filed on January 15, 2021 with the 20 claims that eventually issued into the '023 patent. ECF No. 9-22, Shrestha Decl. Ex. V, '587 Application Prosecution History ("'587 PH"), Transmittal of New Application (BION-ESOL-00038360); *id.* at Original Application at claims (BION-ESOL-00038377-78).

18. On April 19, 2021, the Examiner issued the first and only Office Action, in which all twenty pending claims were rejected: (1) as being obvious over the prior art; and (2) on obviousness-type double patenting grounds over several of the First and Second Wave Patents (the '008, '745, '868, '482, and '621 patents) and over another patent in the same family (U.S. Patent No. 10,799,476). ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, Apr. 19, 2021 Office Action 1-12 (BION-ESOL-00038445-456).

19. Regarding the obviousness-type double patenting rejection, the Examiner stated the following:

> Claims of the '008, '745, '868, '482, '476, and ,621 [sic] are generally drawn towards stable oral liquid formulations comprising enalapril, a buffer comprising citric acid and sodium citrate dehydrate [sic]; a preservative, sweetener and water; wherein the pH of the formulation is less than about 3.5 or about 4.0; wherein the formulation is stable at about 5±3 °C for at least 18 months-24 months. Claims of the '008, '745, '868, '482, '476, and ,621 [sic], all specify the inclusion of the buffer in their system, which is implied in the instant claims in claims which recite the pH requirement of the composition. Thus, claims of '008, '745, '868, '482, '476, and ,621 [sic] of [sic] drawn to a species of the instantly claimed formulation. The ordinarily skilled artisan would find it prima facie obvious to arrive at the instantly claimed invention in view of the compositions described in the claims of '008, '745, '868, '482, '476, and ,621 [sic][.]
>
> Accordingly, the instantly claimed invention is an obvious variant of the invention claimed in '008, '745, '868, '482, '476, and ,621 [sic][.]

Id. at 11 (BION-ESOL-00038455).

20. On April 23, 2021, Azurity submitted its response to the April 19, 2021 Office Action in which it did not amend any application claims but, in response to the Examiner's obviousness rejection, argued that prior art asserted by the Examiner did not teach all the elements of formulations recited in the application claims. ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, Apr. 23, 2021 Response to Non-Final Office Action Dated April 19, 2021 ("April 23, 2021 Response") at 1-8 (BION-ESOL-00038469-476). Azurity also argued (in response to the obviousness rejection) that the stability elements of the claims were not discussed or suggested and that the "superior stability yielded by the claimed formulations are unexpected in view of the cited art." *Id*. at 8-9 (BION-ESOL-00038476-77). Azurity also asserted that "stability of the present formulations is described in the instant specification and drawings, e.g., Tables El and E2." *Id*. at 6 (BION-ESOL-00038474).

21. In support of its arguments regarding unexpected results, Azurity submitted a declaration dated April 23, 2021 from Dr. Gerold Mosher, one of the named inventors. ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, Apr. 23, 2021 Decl. of Gerold Mosher ("Apr. 23, 2021 Mosher Decl.") (BION-ESOL-00038480-88). Azurity argued that the April 23, 2021 Mosher Declaration allegedly shows that "exemplary formulations" as claimed are stable for 12 weeks (total impurity content for these formulations were less than 1% when stored at 5 °C for 12 weeks and less than 2.5% when stored at 25 °C for 12 weeks). ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, Apr. 23, 2021 Resp. at 6 (BION-ESOL-00038474). The "exemplary formulations"—V-3.0, V-3.3, V-3.5, X-1 and X-2 (reproduced below)—were not disclosed in the common specification, but were presented in the April 23, 2021 Mosher Declaration for the first time.

TABLE 1

Composition of Enalapril Maleate Formulations					
Liquid Formulations (mg/mL)					
Component	V-3.0	V-3.3	V-3.5	X-1	X-2
Enalapril maleate	1.00	1.00	1.00	1.00	1.00
Methylparaben				1.80	1.80
Propylparaben				0.20	0.20
Sodium benzoate	1.00	1.00	1.00		
Sodium saccharin					2.0
Sucralose	0.70	0.70	0.70	0.70	
Mixed berry flavor	0.50	0.50	0.50	0.50	0.50
5N HCL/NaOH for pH adjustment	As needed	As needed	As needed	As needed	As needed
Purified water	qs	qs	qs	qs	qs
pH (measured)	3.03	3.33	3.50	3.31	3.31

Id.; ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, Apr. 23, 2021 Mosher Decl. at 4 (BION-ESOL-00038483). Unlike the enalapril liquids described in the common specification, the "exemplary formulations" described in Table 1 of the April 23, 2021 Mosher Declaration do not include a separate, independent buffer component. *Id.* Moreover, the stability data provided for the "exemplary formulations" of the April 23, 2021 Mosher Declaration only goes out to 12 weeks, not to 12 months or longer, as required by the '587 application claims. *Id.* at 5-6 (BION-ESOL-00038484-85). Instead of providing stability data for 12 months or longer for these "exemplary formulations," Dr. Mosher carried out an extrapolation of the 12 week data out to 12 months (*id.* at 8-9 (BION-ESOL-00038487-88)), which, as I explain below, is scientifically improper. Azurity then relied on that extrapolation to argue that the "['exemplary formulations'] demonstrate little loss of enalapril for at least 12 months at 5 °C," and that this allegedly showed that the formulations of the application claims exhibited unexpected stability. ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, Apr. 23, 2021 Resp. at 9 (BION-ESOL-00038477).

22. In response to the Examiner's obviousness-type double patenting rejection, Azurity stated the following in its April 23, 2021 Response:

> Without acquiescing to the merit of the rejection and solely to expedite prosecution, [Azurity] hereby submits terminal disclaimers with respect to U.S. Patent No. 9,669,008, U.S. patent No. 10,039,745, US 10,772,868, US Patent No. 10,786,482, US Patent No. 10,799,476, US patent No [sic], 10,918,621.

ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, Apr. 23, 2021 Resp. at 10 (BION-ESOL-00038478); *see also, id*. at Apr. 23, 2021 Terminal Disclaimer (BION-ESOL-00038491-92).

23. On May 18, 2021, all 20 application claims were allowed. ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, May 18, 2021 Notice of Allowance (BION-ESOL-00038531-32); *id*. at Notice of Allowability (BION-ESOL-00038535-39).

VI. AZURITY'S EPANED®

24. At paragraphs 42-43 of my April 19, 2021 Declaration (Ex. C hereto), I describe the composition of Epaned®, and I incorporate those opinions as fully set forth herein. *See also*, ECF No. 9-7, Shrestha Decl. Ex. G, D. Del. 18-1962 ECF No. 257, Op. at 6.

VII. BIONPHARMA'S ANDA PRODUCT

25. I have described Bionpharma's ANDA product at paragraph 44 of my April 19, 2021 Declaration (Ex. C hereto), and at paragraphs 91-94 of my First Wave Rebuttal Report (Ex. A to Ex. C hereto), and I incorporate those opinions by reference as if set forth herein. *See also* ECF No. 9-7, Shrestha Decl. Ex. G, D. Del. 18-1962 ECF No. 257, Op. at 8.

VIII. LEGAL STANDARDS

26. I have previously been instructed on general legal principles concerning patents, priority claims, and the person of ordinary skill in the art ("POSA"), and legal standards pertaining to: (1) claim construction; (2) direct infringement, including literal infringement, infringement under the doctrine of equivalents, and legal bars to infringement under the doctrine of equivalents;

(2) indirect infringement; and (3) certain invalidity defenses (or requirements for patentability), including obviousness, written description, and enablement, and my understanding of those legal principles and standards is set forth in paragraphs 45-60 of my April 19, 2021 Declaration (Ex. C hereto), and in paragraphs 67-85 in by First Wave Rebuttal Report (Ex. A to Ex. C hereto), which I hereby incorporate as if fully set forth herein.

A. Anticipation

27. I have been advised by counsel for Bionpharma that a patent claim is "anticipated," and therefore invalid, if a single prior art reference discloses each and every limitation of the claimed invention, either expressly or implicitly.

28. I have further been advised that a claim covering a genus of compounds or compositions may be anticipated by a prior art reference that discloses a species falling within the claimed genus.

B. Claim Preclusion

29. I have been advised by counsel for Bionpharma that, pursuant to the doctrine of claim preclusion, a plaintiff cannot sue a defendant on the same cause of action that the parties litigated in a prior suit and that was adjudicated fully on the merits in that prior suit. I have been advised that, for claim preclusion to apply, there must be: (a) a final adjudication on the merits in a prior suit involving (b) the same parties or their privies and (c) a subsequent suit based on the same cause of action. I have also been advised that claim preclusion bars the re-assertion of not only claims that were actually asserted and adjudicated in a prior suit, but also claims that could have been, but were not, asserted in the previous suit.

30. I have further been advised that, in the patent context, claim preclusion usually applies to bar the assertion of the same patent against the same party and the same subject matter.

31. I have further been advised that claim preclusion can also apply to bar the assertion of a different patent from one that was litigated previously between the same parties. Specifically, I have been advised that an adjudication on the merits with respect to a first patent in a previous suit will bar a subsequent suit alleging infringement of a second, different patent (such as a continuation patent) if assertion of the different patent represents the same cause of action that was adjudicated in connection with the previous suit. I have further been advised that, for a cause of action to be the same as one previously asserted, the accused activity between the previous and subsequent suits must be essentially the same, and that, in the patent context, that means that the accused product or process must be essentially the same, and the asserted patent rights must be essentially the same. The patent rights asserted in a subsequent suit are essentially the same as those asserted in a previous suit, I have been advised, if the claims of the asserted patents in the subsequent suit are "patentably indistinct" from the claims of the asserted patents in the previous suit. Finally, I have been advised that a patent claim in a second patent (such as a continuation patent) is patentably indistinct from a patent claim in a first patent if that claim in the first patent anticipates, or renders obvious, the patent claim in the second patent.

IX. CLAIM CONSTRUCTION

32. I have been advised by counsel for Bionpharma that the parties have not yet proposed any terms from the claims of the '023 patent for construction. I have also previously been advised that terms in a claim are generally given their ordinary and customary meaning to a POSA at the time of the alleged invention in view of the claim language itself, other claims, the specification, and prosecution history of the patent. *See, e.g.*, Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶¶ 46-50. Therefore, in rendering my opinions on the claims of the '023 patent, I apply the plain and ordinary meaning to the words in those claims.

33. I have previously been advised by counsel for Bionpharma that one term used in the claims of the '023 patent, "consisting essentially of," has special meaning in patent parlance as a matter of law. *See, e.g.*, Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶ 205. I have been advised that "consisting essentially of, "as used in the claims of the '023 patent, is referred to as a "transitional phrase," because it connects the preamble of the claims (*e.g.*, "A stable oral liquid formulation" for '023 patent claim 1) with the remainder of the claim (referred to as the "body" of the claim). I have previously been advised that "consisting essentially of" means that the claims contain the recited components and anything else that does not materially affect the basic and novel characteristics of the claimed subject matter, and I will apply that meaning throughout my opinions herein.

X. OPINIONS

A. Person of Ordinary Skill in the Art

34. In my First Wave Rebuttal Report (Ex. A to Ex. C hereto), I propounded a definition of the POSA with respect to the First Wave Patents, and I adopted that same definition with respect to the Second Wave Patents. Ex. C, 19-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶ 69. That definition is equally applicable with respect to the '023 patent and I hereby incorporate paragraphs 89-90 of my First Wave Rebuttal Report (Ex. A to Ex. C hereto) as if fully set forth herein.

B. Technical Background: Pharmaceutical Formulation, Acid-Base Chemistry, and Buffers

35. In connection with the First Wave Suits, I provided a tutorial on pharmaceutical formulation, acid-base chemistry, and buffers, both in my First Wave Rebuttal Report and at trial. I hereby incorporate by reference those opinions as if fully set forth herein. *See* Ex. C, 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. Ex. A, First Wave Rebuttal Report at ¶¶ 95-116; Ex.

A, D. Del. 18-1962 ECF No. 195, Trial Tr. Vol. B at Moreton 374:12-375:21; Ex. B, D. Del. 18-1962 ECF No. 196, Sealed Trial Tr. Vol. B at Moreton 515:7-527:17. I note that much of my tutorial opinion was adopted by the Delaware court in its factual findings after trial in the First Wave Suits. *See* ECF No. 9-7, Shrestha Decl. Ex. G, Op. at 9-15, 37-44.

C. The '023 Patent Covers Epaned®

36. I have been asked by counsel for Bionpharma to opine on whether any of the claims of the '023 patent cover Epaned®. It is my opinion that at least several do. For example, as demonstrated below, the formulation elements of claim 1 of the '023 patent read on Epaned®:

Formulation Elements of Claim 1 of the '023 Patent	Epaned® Composition
Claim 1. A stable oral liquid formulation, consisting essentially of:	Epaned® is an oral solution
(i) about 0.6 to about 1.2 mg/ml enalapril or a pharmaceutically acceptable salt or solvate thereof;	1.00 mg/mL enalapril maleate USP
(ii) a sweetener	0.70 mg/mL Sucralose, NF
	1.82 mg/mL citric acid, anhydrous USP
	0.15 mg/mL sodium citrate, dihydrate USP
(iii) a preservative, wherein the preservative comprises sodium benzoate, a paraben or a mixture of parabens;	1.00 mg/mL sodium benzoate, NF
(iv) water, and	Purified water, USP (qs to 1.0 mL)
(v) optionally a flavoring agent;	0.50 mg/mL mixed berry flavor
	Sodium hydroxide (~1% solution) (as required)
	Diluted hydrochloric acid (10% solution) (as required

Compare ECF No. 1-1, Compl. Ex. A, '023 patent at claim 1, *with* ECF No. 9-7, Shrestha Decl. Ex. G, D. Del. 18-1962 ECF No. 257, Op. at 6.

37. Epaned includes a citrate buffer, while the claims of the '023 patent do not expressly recite a buffer. However, the enalapril liquids claimed in the '023 patent may include (and likely include, in the case of those claims that specify pH) a buffer component. This is so because of the "consisting essentially of" transitional-phraseology used in the claims of the '023 patent, which, I have been advised, means the claimed formulations contain the recited ingredients and any others that do not materially affect the basic and novel characteristics of the claimed subject matter. The allegedly novel and basic characteristic of the formulations of the '023 patent is stability, which is expressly required in each claim of the '023 patent (as is the case with all the claims of the First and Second Wave Patents). *See, e.g.*, ECF No. 1-1, Compl. Ex. A, '023 patent at 18:48-19:48; *id*. at claims. The 1.82 mg/mL citric acid and 0.15 mg/mL sodium citrate buffer contained in Epaned® would not be expected to materially affect the stability claimed in the '023 patent—to the contrary, the expectation is that the buffer would contribute to the stability. This is so because the citrate buffer used in Epaned® maintains the formulation pH between about 3.1 to about 3.5. ECF No. 9-7, Shrestha Decl. Ex. G, D. Del. 18-1962 ECF No. 257, Op. at 7. The common specification explains that at a pH of above 3.5, enalapril degradation into enalaprilat increases, and that below a pH of 4 enalapril degradation into enalapril diketopiperazine increases. ECF No. 1-1, Compl. Ex. A, '023 patent 14:41-45. Moreover, as I explained in my April 19, 2021 Declaration (Ex. C hereto), a POSA reading the examples in the common specification would understand that the only formulations reported to be stable at 12 months or longer under

refrigerated conditions (E1-E6)[2] had pHs between 3-3.5, and that the example formulations at higher pHs (*e.g.*, the Example A2-A6 and Example C formulations) likely were not stable for 12 months under refrigerated conditions. *Id*. at Examples A-E; Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶ 155. And the formulation of Epaned is very similar to the E5 and E6 formulations in the common specification, which were demonstrated to be stable at 12 months under refrigerated conditions. ECF No. 1-1, Compl. Ex. A, '023 patent at Example E. Thus, the claims of the '023 patent would not exclude the citrate buffer used in Epaned®.

38. Furthermore, I note that the independent claims of the First Wave Patents all contain a citrate buffer limitation that covers the citrate buffer used in Epaned®, and those claims expressly require stability for at least 12 months under refrigerated conditions. Thus, according to Azurity, who filed for the First Wave Patents, the citrate buffer in Epaned® would not adversely impact the claimed stability.

39. The sodium hydroxide and hydrochloric acid identified in the composition statement for Epaned® are used during the formulation process to adjust pH to an optimal range where enalapril is stable (3-3.5, according to the common specification, as I explained in my April 19, 2021 Declaration (Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶ 155)). Neither may be present in the final formulation of Epaned®. Because the sodium hydroxide and hydrochloric acid used to prepare Epaned® would not be expected to adversely impact stability

[2] As I discuss further below, in my April 19, 2021 Declaration, I opined that the only formulations described in the common specification as being stable for 12 months or longer under refrigerated conditions were the E5 and E6 formulations. *See, e.g.*, Ex. C, Apr. 19, 2021 Moreton Decl. ¶ 139. In fact, as I explain further below, while Example E does not provide 12-month stability data for the E1, E2, E3, and E4 formulations, it does provide data showing that those formulations were stable under refrigerated conditions for 62 weeks, and a POSA would thus reasonably assume that those same formulations were stable under refrigerated conditions for 52 weeks (12 months).

(they would, in fact, contribute to it if used to adjust formulation pH to 3-3.5, as they are used in connection with Epaned®), they are not excluded from the claims of the '023 patent.

40. Finally, Azurity has listed the '023 patent in the FDA's Orange Book for Epaned®, which, counsel for Bionpharma has explained to me, means Epaned® must be stable (as defined in the claims of the '023 patent) under refrigerated conditions for at least 12 months, which is required by all claims of the '023 patent. Thus, at least claim 1 of the '023 patent covers Epaned®.

41. For the same reasons, claims 4 (pH between about 3-4 for at least 3 months under refrigerated conditions), 5 (pH between about 3-4 for at least 12 months under refrigerated conditions), 6 (sweetener is sucralose), 7 (sucralose present in about 0.5-0.9 ml/mL), 10 (flavoring agent), 11 (1.0 mg/mL enalapril or pharmaceutically acceptable salt or solvate), 17 (preservative is sodium benzoate), and 18 (sodium benzoate present between about 0.2-1.2 mg/mL) would also cover Epaned®.

D. Claim Preclusion Should Bar Azurity's Assertion of the '023 Patent

42. I have been asked by Bionpharma to assess whether claim preclusion should bar Azurity's assertion of the '023 patent against Bionpharma, in view of the First and Second Wave Suits. As I explain further below, it is my opinion that claim preclusion should bar the instant suit.

43. For purposes of this analysis, I have been asked by counsel for Bionpharma to assume: (a) that the First and Second Wave Suits were fully adjudicated on the merits; and (b) that the parties (or their privies) to the First and Second Wave Suits are the same parties to the instant action. Thus, I have been asked to focus my analysis on the question of whether Azurity asserts the same "cause of action" in the instant suit that was previously asserted against Bionpharma in the First and Second Wave Suits. I have been advised that the same ANDA—Bionpharma's ANDA No. 212408—that was at issue in the First and Second Wave Suits is at issue in the instant suit. As such, I have been asked to focus my analysis on whether essentially the

same patent rights that were asserted in the First and Second Wave Suits are being asserted in the instant suit.

44. As explained below, it is my opinion that the patent rights asserted in the instant Third Wave Suit are essentially the same as the patent rights that were asserted in connection with the First and Second Wave Suits, as the claims of the ’023 patent are patentably indistinct from the claims of the First and Second Wave Patents.

1. Claim 1 is Anticipated by Claims of the First and Second Wave Patents

45. Claim 1 of the ’023 patent is anticipated by several claims from the First and Second Wave Patents, and is therefore patentably indistinct from those claims. For instance, as I demonstrate below, claim 1 of the ’023 patent is anticipated by claim 1 of the ’868 patent (one of the Second Wave Patents):

Claim 1 of the ’023 Patent	**Claim 1 of the ’868 Patent (with elements rearranged to match relevant limitations of ’023 patent claim 1)**
Claim 1. A stable oral liquid formulation, consisting essentially of:	Claim 1. A stable oral liquid formulation, consisting essentially of:
(i) about 0.6 to about 1.2 mg/ml enalapril or a pharmaceutically acceptable salt or solvate thereof;	(i) about 0.6 to about 1.2 mg/ml enalapril or a pharmaceutically acceptable salt or solvate thereof;
(ii) a sweetener	wherein the formulation optionally comprises a sweetener, a flavoring agent, or both;
	(ii) a buffer to maintain the pH about 4.5 or below, wherein the buffer concentration is about 5 mM to about 20 mM;
(iii) a preservative, wherein the preservative comprises sodium benzoate, a paraben or a mixture of parabens;	(iii) about 1 mg/ml of a preservative that is sodium benzoate; and
(iv) water, and	(iv) water,

(v) optionally a flavoring agent;	wherein the formulation optionally comprises a sweetener, a flavoring agent, or both;
wherein the formulation is stable at about 5±3° C. for at least 12 months; and	wherein the formulation is stable at about 5±3° C. for at least 12 months; and
wherein the stable oral liquid formulation has about 95% w/w or greater of the initial enalapril amount and about 5% w/w or less total impurity or related substances at the end of the given storage period.	wherein the stable oral liquid formulation has about 95% w/w or greater of the initial enalapril amount and about 5% w/w or less total impurity or related substances at the end of the given storage period.

ECF No. 1-1, Compl. Ex. A, '023 patent at claim 1; ECF No. 9-11, Shrestha Decl. Ex. K, '868 patent at claim 1. As can be seen, claim 1 of the '868 patent discloses each and every limitation of claim 1 of the '023 patent.

46. Of course, Claim 1 of the '868 patent discloses a limitation not expressly present in claim 1 of the '023 patent: "a buffer to maintain the pH about 4.5 or below, wherein the buffer concentration is about 5 mM to about 20 mM." As I've explained above, a buffer that maintains the pH of the enalapril liquid between 3-3.5 would be expected to contribute to the stability of the liquid. However, the buffer element of claim 1 of the '868 patent permits a buffer that maintains a pH outside of the 3-3.5 range. As I explain below, there is simply no description in the common specification of an enalapril liquid with a pH outside of 3-3.5 that is stable for at least 12 months under refrigerated conditions (5±3° C.). Nevertheless, claim 1 of the '868 patent itself requires that the claimed buffer not adversely impact stability, as all formulations of that claim are required to be stable for at least 12 months under refrigerated conditions (just as the formulations claimed in claim 1 of the '023 patent). Thus, claim 1 of the '023 patent would not exclude the formulations of claim 1 of the '868 patent, which contain a "a buffer to maintain the pH about 4.5 or below, wherein the buffer concentration is about 5 mM to about 20 mM." Claim 1 of the '868 patent essentially recites a subgenus of the formulations covered by claim 1 of the '023 patent. Thus,

claim 1 of the '868 patent anticipates claim 1 of the '023 patent, and claim 1 of the '023 patent is therefore patentably indistinct from claim 1 of the '868 patent.

47. Similarly, as I demonstrate below, claim 1 of the '023 patent is anticipated by claim 2 of the '745 patent (one of the First Wave Patents):

Claim 1 of the '023 Patent	**Claim 2 of the '745 Patent (with claim 1 elements incorporated and certain elements rearranged to match relevant limitations of '023 patent claim 1)**
Claim 1. A stable oral liquid formulation, consisting essentially of:	[Claim 1.] A stable oral liquid formulation, comprising:
(i) about 0.6 to about 1.2 mg/ml enalapril or a pharmaceutically acceptable salt or solvate thereof;	(i) about 0.6 to about 1.2 mg/ml enalapril or a pharmaceutically acceptable salt or solvate thereof;
(ii) a sweetener	Claim 2. The stable oral liquid formulation of claim 1 further comprising about 0.5 to about 0.9 mg/ml sucralose
	(ii) a buffer comprising about 0.8 to about 3.5 mg/ml citric acid and about 0.1 to about 0.8 mg/ml sodium citrate;
(iii) a preservative, wherein the preservative comprises sodium benzoate, a paraben or a mixture of parabens;	(iii) about 0.7 to about 1.2 mg/ml sodium benzoate; and
(iv) water, and	(iv) water,
(v) optionally a flavoring agent;	
wherein the formulation is stable at about 5±3° C. for at least 12 months; and	wherein the formulation is stable at about 5±3° C. for at least 12 months; and
wherein the stable oral liquid formulation has about 95% w/w or greater of the initial enalapril amount and about 5% w/w or less total impurity or related substances at the end of the given storage period.	wherein the stable oral liquid formulation has about 95% w/w or greater of the initial enalapril amount and about 5% w/w or less total impurity or related substances at the end of the given storage period.

ECF No. 1-1, Compl. Ex. A, '023 patent at claim 1; ECF No. 9-5, Shrestha Decl. Ex. E, '745 patent at claims 1-2. Claim 2 of the '745 patent implies that the claimed buffer ("a buffer comprising about 0.8 to about 3.5 mg/ml citric acid and about 0.1 to about 0.8 mg/ml sodium citrate") would not adversely impact stability, as all formulations falling within the scope of claim 2 are required to be stable for at least 12 months under refrigerated conditions. Thus, claim 2 of the '745 patent essentially recites a subgenus of the enalapril liquids claimed in claim 1 of the '023 patent. As such, claim 2 of the '745 patent anticipates claim 1 of the '023 patent, and claim 1 of the '023 patent is therefore patentably indistinct from claim 2 of the '745 patent.

48. Finally, I note that numerous other claims of the First and Second Wave Patents anticipate claim 1 of the '023 patent, including claim 19 of the '008 patent, claims 3 and 17 of the '442 patent, claims 2 and 19 of the '987 patent, claim 15 of the '482 patent, and claims 1, 19, and 30 of the '621 patent. As with claim 1 of the '868 patent, and claim 2 of the '745 patent, each of those claims recites a subgenus of the formulations covered by claim 1 of the '023 patent, and they each therefore anticipate claim 1 of the '023 patent, rendering it patentably indistinct from those claims.

2. Claims 2 and 3 ("the Extended Stability Claims") Are Anticipated by Claims of the First and Second Wave Patent Claims

49. Claim 2 of the '023 patent requires stability under refrigerated conditions for at least 18 months, while claim 3 of the '023 patent requires such stability for at least 24 months. ECF No. 1-1, Compl. Ex. A, '023 patent at claims. Claims 11 and 12 of the '868 patent—which each depend from claim 1 of the '868 patent and require 18 month and 24 month stability under refrigerated conditions, respectively—anticipate these claims, as they disclose each and every limitation of claims 2 and 3 of the '023 patent. ECF No. 9-11, Shrestha Decl. Ex. K, '868 patent

at claims. As such, the Extended Stability Claims are patentably indistinct from at least claims 11 and 12 of the '868 patent.

3. Claims 4 and 5 ("the pH Range Claims") Are Anticipated by the First and Second Wave Patent Claims

50. Claim 4 of the '023 patent depends from claim 1 and requires that the formulation pH be maintained between about 3-4 for at least 3 months under refrigerated conditions, while claim 5 also depends from claim 1 and requires that the formulation maintain the same pH for at least 12 months under refrigerated conditions ("the pH Range Claims"). ECF No. 1-1, Compl. Ex. A, '023 patent at claims. Both claims are anticipated by, for example, claim 10 of the '868 patent, which depends from claim 1 of the '868 patent and requires additionally that the buffer maintain the pH at about 3.3. ECF No. 9-11, Shrestha Decl. Ex. K, '868 patent at claims. The POSA would understand from claim 10 of the '868 patent that the buffer would inherently maintain the required pH (about 3.3) for at least 12 months, because claim 1 of the '868 patent (from which claim 10 depends) requires stability under refrigerated conditions for at least 12 months. A POSA would understand that for the formulation to be stable, the pH would need to be maintained between about 3-3.5 for the duration of the stability limitation (12 months). Thus, it is my opinion that at least claim 10 of the '868 patent anticipates claims 4 and 5 of the '023 patent, and therefore those claims are patentably indistinct from at least claim 10 of the '868 patent.

51. For essentially the same reasons, a number of other claims of the First and Second Wave Patents would anticipate claims 4 and 5 of the '023 patent, including claim 9 of the '868 patent, and claims 6 and 7 of the '621 patent. ECF No. 9-13, Shrestha Decl. Ex. M, '621 patent at claims.

52. Alternatively, claims 4 and 5 of the '023 patent would be obvious from at least claim 10 of the '868 patent, and claims 6 and 7 of the '621 patent. Although those claims do not

expressly recite pH maintenance for at least 3 months ('023 patent claim 4) or 12 months ('023 patent claim 5) under refrigerated conditions, the POSA would know well that the pH of the formulations falling within those claims must be maintained for at least 12 months. Moreover, it would be unheard of for a formulator to develop a formulation with a buffer to maintain pH for a period less than the normal shelf life of the formulated product—usually at least 24 months. Indeed, the whole point of maintaining the formulation pH of enalapril liquids to a range between 3-3.5 would be to maintain stability for the shelf-life of the liquid, and POSA would know that. Thus, claims 4 and 5 of the '023 patent are patentably indistinct from at least claim 10 of the '868 patent, and claims 6 and 7 of the '621 patent.

4. Claims 6 and 7 ("the Sucralose Claims") Are Anticipated by the First and Second Wave Patent Claims

53. As explained above, claim 2 of the '745 patent depends from claim 1 of that patent and specifies the inclusion of "about 0.5 to about 0.9 mg/ml sucralose." ECF No. 9-5, Shrestha Decl. Ex. E, '745 patent at claims 1-2. Claim 2 of the '745 patent thus anticipates claims 6 and 7 of the '023 patent, which each depend from claim 1 of the '023 patent (directly or indirectly) and require inclusion of sucralose (claim 6) or sucralose at about "about 0.5 to about 0.9 mg/ml" (claim 7). Thus, the Sucralose Claims are patentably indistinct from the claims of the First and Second Wave Patents.

5. Claims 8 and 9 ("the Saccharin Claims") Are Obvious in View of the First and Second Wave Patent Claims

54. While certain claims of the First and Second Wave Patents recite enalapril liquids with sweeteners (*e.g.*, claim 1 of the '868 patent (as shown above), and claims 1 and 19 of the '621 patent), and with sucralose specifically as a sweetener and at a specific concentration range (*e.g.*,'868 patent claim 3; '745 patent claim 2), none of the claims of the First and Second Wave

Patents recite saccharin specifically as a sweetener. However, it is common knowledge in and outside of the pharmaceutical drug industry that saccharin is a sweetener used in beverages, food and medicinal products. *See, e.g.*, Ex. E, RAYMOND C. ROWE ET AL., HANDBOOK OF PHARMACEUTICAL EXCIPIENTS 605-610 (6th Ed. 2009) ("HPE"). The POSA would readily know this, and know that saccharin and its salts could be used interchangeably for sucralose. *Id*. Indeed, the common specification identifies sucralose as a suitable sweetener for use in the claimed enalapril liquids. *See, e.g.*, ECF No. 9-3, Shrestha Decl. Ex. C, '008 patent 8:27-32.

55. Thus, it is my opinion that a POSA would find claim 8 obvious over any of claims 1 and 3 of the '868 patent, claim 2 of the '745 patent, and claims 1 and 19 of the '621 patent. Claim 9 requires the presence of saccharin (or its salt) at a concentration of "about 2 mg/ml." In my opinion, it would have required nothing more than routine experimentation to arrive at this concentration. A POSA following, for instance, claim 1 of the '868 patent, which calls for an optional sweetener, would look at the other required components (0.6-1.2 mg/ml enalapril or salt/solvate, 5-20 mM of a buffer, and 1 mg/ml sodium benzoate), and would easily be able to arrive at the "about 2 mg/ml" required by claim 9 of the '023 patent. Thus, claim 9 would also be obvious in view of claim 1 of the '868 patent (as well as claim 3 of the '868 patent, claim 2 of the '745 patent, and claims 1 and 19 of the '621 patent).

6. Claims 10-12, 17-18, and 20 Are Anticipated by the First and Second Wave Patent Claims

56. Claim 20 of the '023 patent depends from claim 1 and narrows the enalapril, sweetener, and preservative limitations. As I demonstrate below, claim 20 is anticipated by at least claim 18 of the '008 patent:

Claim 20 of the '023 Patent vritten to incorporate claim 1 elements)	**Claim 18 of the '008 Patent (with elements rearranged to correspond to relevant limitations of '023 patent claim 20)**

Claim 20. The stable oral liquid formulation of claim 1, consisting essentially of:	Claim 18. A stable oral liquid formulation, consisting essentially of:
(i) about 1.0 mg/ml enalapril or a pharmaceutically acceptable salt or solvate thereof;	(i) about 1 mg/ml enalapril maleate;
(ii) a sweetener that is sucralose or sodium saccharin;	(ii) about 0.70 mg/ml of a sweetener that is sucralose;
	(iii) a buffer comprising about 1.82 mg/ml citric acid and about 0.15 mg/ml sodium citrate dihydrate;
(iii) a preservative, wherein the preservative comprises sodium benzoate that is present at about 0.2 mg/ml to about 1.2 mg/ml in the oral liquid formulation;	(iv) about 1 mg/ml of a preservative that is sodium benzoate;
(iv) water, and	(vi) water,
(v) optionally a flavoring agent;	(v) a flavoring agent;
	wherein the pH of the formulation is less than about 3.5 adjusted by sodium hydroxide or hydrochloric acid if needed; and
wherein the formulation is stable at about 5±3° C. for at least 12 months; and	wherein the formulation is stable at about 5±3° C. for at least 12 months;
wherein the stable oral liquid formulation has about 95% w/w or greater of the initial enalapril amount and about 5% w/w or less total impurity or related substances at the end of the given storage period.	wherein the stable oral liquid formulation has about 95% or greater of the initial enalapril amount and about 5% w/w or less total impurities or related substances at the end of the given storage period.

ECF No. 1-1, Compl. Ex. A, '023 patent at claim 20; ECF No. 9-3, Shrestha Decl. Ex. C, '008 patent at claim 18. Claim 18 of the '008 patent not only discloses each and every limitation of claim 20 of the '023 patent, claim 18 of the '008 patent essentially describes a subgenus of the formulations claimed in claim 20 of the '023 patent. Thus, claim 20 of the '023 patent is patentably indistinct from claim 18 of the '008 patent. I note that claim 20 of the '023 patent is anticipated

by other claims of the First and Second Wave Patents, including at least claim 19 of the '008 patent.

57. For essentially the same reasons, claim 18 of the '008 patent also anticipates '023 patent claim 10, which depends from claim 1 and requires a flavoring agent; claim 12, which depends from claim 1 and requires 1.0 mg/ml of enalapril or its salt/solvate; claim 17, which depends from claim 1 and requires sodium benzoate as the preservative; and claim 18, which depends from claim 17 and requires sodium benzoate at a concentration of about 0.2-1.2 mg/ml. ECF No. 1-1, Compl. Ex. A, '023 patent at claims; ECF No. 9-3, Shrestha Decl. Ex. C, '008 patent at claim 18. Thus, it is my opinion that claims 10, 12, 17, and 18 are patentably indistinct form the First and Second Wave Patent Claims.

58. Next, it is my opinion that '023 patent claim 11 is also anticipated by at least claim 18 of the '008 patent. Claim 11 of the '023 patent depends from claim 1 and specifies that "the enalapril or a pharmaceutically acceptable salt or solvate thereof functions as a buffer." ECF No. 1-1, Compl. Ex. A, '023 patent at claim 11. As I explain in detail below, there is no description in the common specification of any liquid formulation where enalapril or its pharmaceutically acceptable salt of solvate "functions as a buffer." Nor is there any evidence, description, or even suggestion in the common specification that enalapril or its pharmaceutically acceptable salt or solvate can function as a buffer in a liquid formulation. The first mention or suggestion of this is in the April 23, 2021 Mosher Declaration submitted during prosecution of the '587 application, where Dr. Mosher states that "[f]ormulations of Table 1 do not require additional buffering agents other than enalapril maleate, which is a salt of an amino acid. As an amino acid, an enalapril molecule contains carboxylic acid and amine groups that can dissociate and thus balance the pH

variations." ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, Apr. 23, 2021 Mosher Decl. at 5 (BION-ESOL-00038484).

59. From Dr. Mosher's own statement during prosecution, it appears that Azurity has tried to claim in claim 11 of the '023 patent an inherent property of enalapril or its pharmaceutically acceptable salt or solvate in a liquid formulation. I have been advised by Bionpharma's counsel that an inherent property of a claimed formulation need not be disclosed in a prior art reference for that reference to be anticipatory. If that is the case, it is my opinion that claim 11 of the '023 patent is anticipated by at least claim 1 of the '868 patent, and is thus patentably indistinct from at least that claim.

60. I further note that, for the same reasons, claim 11 of the '023 patent is anticipated by several other claims of the First and Second Wave Patents, including claims 18 and 19 of the '008 patent, and claims 1 and 19 of the '621 patent.

7. Claims 13-16 and 19 ("the Paraben Claims") Are Anticipated by, or Obvious in View of, the First Wave Patent Claims

61. Claim 16 of the '023 patent depends from claim 1 and specifies that the paraben or paraben mixture is present at about 0.1-2 mg/ml in the formulation. ECF No. 1-1, Compl. Ex. A, '023 patent at claim 16. As demonstrated below, claim 27 of the '621 patent anticipates claim 16 of the '023 patent:

Claim 16 of the '023 Patent vritten to incorporate claim 1 elements)	**Claim 27 of the '621 Patent (rewritten to incorporate claim 19 elements, with elements rearranged to correspond to relevant limitations of '023 patent claim 16)**
Claim 16. A stable oral liquid formulation, consisting essentially of:	[Claim 19.] A stable oral liquid formulation, consisting essentially of:

(i) about 0.6 to about 1.2 mg/ml enalapril or a pharmaceutically acceptable salt or solvate thereof;	(i) about 0.6 to about 1.2 mg/ml enalapril or a pharmaceutically acceptable salt or solvate thereof;
(ii) a sweetener	wherein the formulation optionally comprises a sweetener, a flavoring agent, or both;
	(ii) a buffer to maintain the pH about 4.5 or below, wherein the buffer concentration is about 5 mM to about 20 mM;
(iii) a preservative, wherein the preservative comprises sodium benzoate, [or about 0.1 mg/ml to about 2 mg/ml of] a paraben or a mixture of parabens;	(iii) a preservative, wherein the preservative is methylparaben, ethylparaben, propylparaben, butylparaben, or a combination thereof [Claim 27. . . . wherein the preservative is present at about 0.1 mg/ml to about 2 mg/ml]; and
(iv) water, and	(iv) water
(v) optionally a flavoring agent;	wherein the formulation optionally comprises a sweetener, a flavoring agent, or both;
wherein the formulation is stable at about 5±3° C. for at least 12 months; and	wherein the formulation is stable at about 5±3° C. for at least 12 months; and
wherein the stable oral liquid formulation has about 95% w/w or greater of the initial enalapril amount and about 5% w/w or less total impurity or related substances at the end of the given storage period.	wherein the stable oral liquid formulation has about 95% w/w or greater of the initial enalapril amount and about 5% w/w or less total impurity or related substances at the end of the given storage period.

ECF No. 1-1, Compl. Ex. A, ’023 patent at claim 16; ECF No. 9-13, Shrestha Decl. Ex. M, ’621 patent at claim 27. As can be seen above, claim 27 of the ’621 patent not only discloses all of the limitations of ’023 patent claim 16, claim 27 of the ’621 patent recites a subgenus of the formulations of claim 16 of the ’023 patent, and thus anticipates claim 16. Thus, claim 16 of the ’023 patent is patentably indistinct from at least claim 27 of the ’621 patent.

62. Similarly, claim 27 of the ’621 patent anticipates: (i) claim 13, which depends from claim 1 and specifies that the preservative is a mixture of parabens; (ii) claim 14, which depends from claim 1 and specifies that the “paraben or mixture of parabens is methylparaben,

ethylparaben, propylparaben, butylparaben, salts thereof, or a combination thereof"; and (iii) claim 15, which depends from claim 1 and specifies that the mixture of parabens is methylparaben and propylparaben. *Compare* ECF No. 1-1, Compl. Ex. A, '023 patent at claims 13-15, *with* ECF No. 9-13, Shrestha Decl. Ex. M, '621 patent at claim 27. Claim 27 of the '621 patent discloses all of the limitations of claim 1 (as I have demonstrated in the table in the last paragraph), as well as the additional limitations recited in claims 13-15 of the '023 patent. Thus, claims 13-15 of the '023 patent are patentably indistinct from at least claim 27 of the '621 patent.

63. I note that that while '023 patent claims 14, 15, and 16 depend from claim 1, they do not actually require that the preservative be a paraben or mixture of parabens—they only narrow the paraben elements of claim 1. Thus, '023 patent claims 14, 15, and 16 conceivably cover enalapril liquids that contain sodium benzoate as a preservative and no parabens. As such, claims 14, 15, and 16 of the '023 patent are also anticipated by claim 1 of the '868 patent and claim 2 of the '745 patent, as explained above in connection with anticipation of claim 1 of the '023 patent.

64. Claim 19 of the '023 patent depends from claim 1 and further narrows the enalapril, sweetener, and preservative limitations. Claim 19 of the '023 patent is essentially a hybrid of claims 24 and 27 of the '621 patent, which depend from claim 19 of the '621 patent and narrow the enalapril limitation to 1.0 mg/ml enalapril (or salt/solvate) and the paraben preservative limitation to a concentration of about 0.1-2 mg/ml. However, while claims 24 and 27 of the '621 patent disclose the optional use of a sweetener, they do not expressly further narrow that sweetener to sucralose or sodium saccharin, as required by claim 19 of the '023 patent. Nevertheless, the POSA would most certainly know that sucralose and sodium saccharin are sweeteners suitable for use in the enalapril liquids claimed in the '621 patent, particularly in view of other claims of the First and Second Wave Patents that requires sucralose as a sweetener (such as claim 2 of the '745

patent). Thus, it is my opinion that claim 19 of the '023 patent is at least obvious over claims 24 and 27 of the '621 patent, and therefore patentably indistinct from those claims.

E. The '023 Patent Claims Are Invalid

65. In my April 19, 2021 Declaration, I opined that the claims of the Second Wave Patents covered subject matter that Azurity simply did not invent. Specifically, it was my opinion that the claims of the Second Wave Patents covered thousands (and, in some cases, millions) of enalapril liquids that were nowhere described in the common specification as being stable for at least 12 months under refrigerated conditions. *See* Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶¶ 142-169, 207-219, 234-247.

66. I herein reach a similar conclusion with respect to the claims of the '023 patent. As I explain further below, the claims of the '023 patent cover tens (and likely hundreds) of thousands of enalapril liquids nowhere described as being stable for at least 12 months under refrigerated conditions.

67. As I explained in my April 19, 2021 Declaration, in discussing stability of the enalapril liquids disclosed, the common specification discloses that

> **Under refrigerated condition, the enalapril oral liquid formulations described herein are stable for at least 1 month, at least 2 months, at least 3 months, at least 6 months, at least 9 months, at least 12 months, at least 15 months, at least 18 months, at least 24 months, at least 30 months and at least 36 months.**

ECF No. 1-1, Compl. Ex. A, '023 patent 18:54-59; Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶ 138. A POSA would understand this statement as meaning that some enalapril liquids disclosed in the common specification are stable under refrigerated conditions for at least 1 month, while others are stable under refrigerated conditions for at least 2 months, while others are stable under refrigerated conditions for at least 3 months, and so on. A POSA would **not** understand this statement as meaning that all enalapril liquids disclosed in the common

specification are stable under refrigerated conditions for at least 12 months or longer, or that all disclosed formulations are stable under refrigerated conditions for at least 36 months.

68. The only stability data provided at any conditions for 12-months or longer is for the enalapril liquids described at Example E of the common specification. A point of clarification. In my April 19, 2021 Declaration, I suggested that the common specification did not disclose 12-month or longer stability data for any enalapril liquids beyond the data provided for the E5 and E6 liquids described in Example E. *See, e.g.*, Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶ 139. In fact, the common specification provides 62-week stability data for the E1, E2, E3, and E4 formulations described in Example E, but does not provide 52-week (12 month) stability data for those formulations. Nonetheless, because the data provided in Example E shows that the E1, E2, E3, and E4 formulations are stable at 62 weeks, a POSA would reasonably assume that those formulations would also be stable at 12 months (52 weeks).

69. Thus, the only enalapril liquids that are described as being stable for 12 months or longer (at any conditions) are the Example E formulations. However, the Example E formulations are all very similar, as they each contain 1 mg/mL of enalapril maleate, a citric acid/sodium citrate buffer at specific concentrations (about 0.8-3.3 mg/mL of citric acid and about 0.1-0.8 mg/mL of sodium citrate), and 1 mg/mL of sodium benzoate as a preservative. The Example E formulations essentially represent the narrow group of enalapril liquids claimed in Azurity's First Wave Patents. *Compare* ECF No. 1-1, Compl. Ex. A, '023 patent at Example E, *with* ECF No. 9-3, Shrestha Decl. Ex. C, '008 patent at claim 1, *and* ECF No. 9-5, Shrestha Decl. Ex. E, '745 patent at claim 1.

70. As I explained in my April 19, 2021 Declaration, data provided in the common specification for enalapril liquids beyond the Example E liquids suggests that numerous enalapril liquids falling within the scope of the claims of the Second Wave Patents would not meet the

stability limitations of those claims, rendering them—in the opinion of Azurity's own expert in the First and Second Wave Suits, Dr. Stephen Byrn—inoperable. Ex. C, Apr. 29, 2021 Moreton Decl. ¶ 139; Ex. B, D. Del. 18-1962 ECF No. 196, Sealed Trial Tr. Vol. B, Byrn 428:24-429:6; Ex. D, 18-1962 ECF No. 194, Sealed Trial Tr. Vol. A, Byrn 296:19-298:9. Moreover, as I also stated in my April 19, 2021 Declaration, undue experimentation would be required for a POSA to figure out which liquids falling within the scope of claims of the Second Wave Patents are operable and which ones are not. Ex. C, Apr. 29, 2021 Moreton Decl. ¶¶ 170-184, 220-231, 248-261.

71. I reach the same conclusion with respect to the claims of the '023 patent. As I've explained above with respect to claim preclusion, the claims of the '023 patent are very similar to the claims of the Second Wave Patents—in fact, the claims of the '023 patent are essentially slightly broader versions of the claims of the '868 and '621 patents. As with the claims of the '868 and '621 patents, data provided in the common specification for formulations beyond the Example E formulations suggests that numerous formulations falling within the scope of the '023 patent claims would not meet the stability limitations of those claims, rendering them inoperable.

72. Beyond that, the claims of the '023 patent include a genus of enalapril liquids that are not covered by the claims of the Second Wave Patents: enalapril liquids that do not include a separate, independent buffer component that are stable for at least 12 months under refrigerated conditions. As I explain below, this aspect of the '023 patent claims finds absolutely no support in the common specification, and, in my opinion, runs contrary to positions taken by Azurity during trial in the First Wave Suits.

73. It is my opinion that the claims of the '023 patent should never have issued. As I explained in my April 19, 2021 Declaration, during prosecution of the Second Wave Patents, which sought claim coverage beyond the Example E formulations claimed in the First Wave

Patents, the PTO Examiner picked up on the fact that Azurity was trying to claim stable enalapril liquids that were never described in the common specification, and rejected claims of the Second Wave Patents for lack of written description. *See* Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶¶ 15-29, 166-167, and 210-211. In response, Azurity submitted declarations from Dr. Mosher, after the filing of the original applications for the Second Wave Patents, describing new enalapril liquids falling with the scope of the claims of the Second Wave Patents that were nowhere described in the common specification. *Id*. The Examiner accepted those Mosher declarations as support for the Second Wave Patents claims and withdrew the written description rejection under the mistaken belief, I have been advised by Bionpharma's counsel, that a deficient specification could be supplemented by post-application filing date declarations, which Bionpharma's counsel advises me is a violation of fundamental patent law. That same mistake appears to have been made by the PTO Examiner in connection with prosecution of the '587 application, where the Examiner accepted the April 23, 2021 Mosher Declaration, which disclosed enalapril liquids that do not contain a separate, independent buffer component—such formulations, as I explain further below, are nowhere supported in the common specification.

74. Finally, as with claims 14-23 and 27-28 of the '482 patent, and all of the claims of the '621 patent, in the event the Court finds the claims of the '023 patent adequately supported in the common specification, it is my opinion that at least claims 1-16 and 19 of the '023 patent are obvious in view of the prior art, as those claims essentially read on the prior art Epaned® Kit formulation (reconstituted).

1. The '023 Patent Claims Are Not Described in the Common Specification

75. As with the claims of the '868 and '621 patents (which, like the '023 patent claims, use the "consisting essentially of" transitional phraseology), the formulation elements of the claims

of the ’023 patent cover tens (and likely hundreds) of thousands of enalapril liquids. This is so, in part, because the claims of the ’023 patent do not expressly require, but certainly may contain, a buffer, and the claims of the Second Wave Patents tell us that buffers that are suitable for use in enalapril liquids stable for at least 12 months under refrigerated conditions can be “a citrate, a phosphate, a citrate/phosphate, an acetate, a glycinate, an amino acid, or a tartrate buffer.” ECF No. 9-11, Shrestha Decl. Ex. K, ’868 patent at claims. As I explained in by April 19, 2021 Declaration in connection with the claims of the ’868 patent, this means that tens (possibly hundreds) of thousands of buffered enalapril liquids may fall within the formulation elements of the ’023 patent claims. Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶¶ 205-06. Add to that tally all of the enalapril liquids falling within the formulation elements of the ’023 patent claims that do not contain a separate, independent buffer component. I further note that many of the ’023 patent claims contain no restriction on sweetener, preservative, or flavoring agent concentrations, or on formulation pH.

76. Furthermore, the common specification identifies at least 38 different buffering agents, at least 47 different flavoring agents, and approximately 38 different sweeteners. ECF No. 1-1, Compl. Ex. A, ’023 patent 8:45-9:16, 13:35-57, 17:61-18:18. All of these different combinations, at different concentrations, and different pHs, and with different concentrations of enalapril that are permitted (“about 0.6 to about 1.2 mg/ml”), leads to an incredibly large number of enalapril liquids that can meet the formulation elements of the ’023 patent claims. I conservatively put the number at tens of thousands of potential liquids, but it is more likely hundreds of thousands of enalapril liquids that meet the formulation elements of the claims.

77. As I explain below, there are numerous aspects of the '023 patent claims, and numerous enalapril liquids falling within the scope of those claims, that are nowhere described in the common specification.

a. Formulations beyond the Example E Formulations

78. As I have explained above, there are tens (and likely hundreds) of thousands of enalapril liquids falling with the scope of the formulation elements of the '023 patent claims. But the common specification does not provide any description of all of these tens (and likely hundreds) of thousands of liquids falling within the scope of the formulation elements of the '023 patent claims as being stable for 12 months or longer under refrigerated conditions.

79. As I have explained above, the common specification states that the disclosed formulations can be stable under refrigerated conditions "for at least 1 month, at least 2 months, at least 3 months, at least 6 months, at least 9 months, at least 12 months, at least 15 months, at least 18 months, at least 24 months, at least 30 months and at least 36 months." ECF No. 1-1, Compl. Ex. A, '023 patent 19:9-14. Thus, enalapril liquids having stability for 12 months or longer under refrigerated conditions are a subset of the many formulations disclosed in the common specification. With that in mind, the specification only describes a very narrow group of liquids as being stable for 12 months or longer under refrigerated conditions: the Example E liquids (E1, E2, E3, E4, E5, and E6). *Id*. at Example E. As I have explained above, these six enalapril liquids are very similar, as each contains 1 mg/mL of enalapril maleate, a citric acid/sodium citrate buffer at specific concentrations (about 0.8-3.3 mg/mL of citric acid and about 0.1-0.8 mg/mL of sodium citrate), and 1 mg/mL of sodium benzoate as a preservative. There is no other 12-month stability data whatsoever for any other liquid. Nor is there any other disclosure of any other formulation

along with a statement, assertion, or data even suggesting that that formulation is or would be stable for 12 months or longer under refrigerated conditions.

80. Furthermore, certain statements and accelerated data provided in the common specification would suggest that numerous liquids falling within the scope of the '023 patent claims would not be stable for 12 months under refrigerated conditions. For instance, from the stability data provided for the Examples A and C paraben liquids, a POSA would reasonably believe that those liquids would likely not be stable for at least 12 months under refrigerated conditions. Each of the Example C liquids would fall within the literal scope of the formulation elements of many of the '023 patent claims (*e.g.*, claims 1, 6-7, 10, 12-16, and 19).

81. As I explained in my April 19, 2021 Declaration at Paragraph 146, which I incorporate herein by reference, the accelerated data provided for the Example C liquids "provide a POSA with a strong indication that the Example C formulations would likely not meet the stability requirements of any of the claims of the ['023 patent]." Ex. C, Apr. 21, 2021 Moreton Decl. ¶ 146.

82. Moreover, the POSA would understand that some excipients that can be included in the enalapril liquids claimed in the '023 patent (by virtue of the "comprises" transitional phraseology used in the preservative limitations of those claims) could destabilize enalapril. For instance, aqueous solutions of potassium sorbate—an excipient disclosed in the common specification as a suitable preservative for use in the claimed enalapril liquids and in fact used in certain example formulations disclosed (*e.g.*, Example C1 and C2 liquids), ECF No. 1-1, Compl. Ex. A, '023 patent at 10:34-43 and Example C—were known to "rapidly decompose[] when stored in polypropylene, polyvinylchloride, and polyethylene containers," without the addition of antioxidants. Ex. E, HPE at 579 and 673 (potassium sorbate and sorbic acid entries). Such

containers are commonly used to package pharmaceutical oral solutions, including Epaned®, which is packaged in "white, opaque, high-density polyethylene bottled with a white polypropylene, child-resistant closure." Ex. F, Description of Composition for Epaned® (SLVGT-EPA_0003204).

83. Similarly, the common specification itself warns against using paraben preservatives—which are permitted or required in all of the '023 patent claims—with certain sweeteners, such as sugars (such as glucose, fructose, sucrose, lactose, maltose) and certain sugar alcohols (such as xylitol, mannitol, lactitol, maltitol, and sorbitol). ECF No. 1-1, Compl. Ex. A, '023 patent 13:18-31; *id*. at claims. The common specification explains that combining parabens with these types of sweeteners may result in transesterification reaction products, which can be "undesirable from a formulation and stability standpoint as the transesterification creates additional degradants." *Id.* at 13:18-25. However, all of the claims of the '023 patent permit or require paraben preservatives, and at the same time require sweeteners. The POSA reading the common specification would believe numerous paraben preserved enalapril liquids that contain sweeteners and that fall within the formulation elements of the '023 patent claims likely would not be stable under refrigerated conditions for at least 12 months because of the transesterification that the common specification warns of in connection with such formulations.

84. Furthermore, as Azurity's expert in the First and Second Wave Suits, Dr. Byrn, explained in a declaration he submitted in support of Azurity's preliminary injunction motion filed in connection with the Second Wave Suits that enalapril was "known to have stability issues once dissolved into a solution." Ex. G, D. Del. 18-1962 ECF No. 235, Mar. 31, 2021 Decl. of Stephen R. Byrn, Ph.D. in Supp. of Silvergate's Mot. for Prelim. Inj. (" Mar. 31, 2021 Byrn Decl.") ¶ 15.

Dr. Byrn further explains, "a liquid formulation of enalapril would generally be expected to have a short shelf-life (e.g., on the order of weeks to only a few months)." *Id*.

85. In light of the foregoing information from the common specification and a POSA's common knowledge, as evidenced by Dr. Byrn's opinions regarding what was known about enalapril stability in liquid formulations, a POSA would simply not believe that all—or anywhere near all—of the tens (likely hundreds) of thousands of enalapril liquids falling within the scope of the claims of the '023 patent would meet the stability requirements of those claims. Indeed, the POSA would believe, based on at least the data provided for the Example C formulations, common knowledge about the potential destabilizing effects of certain excipients such as potassium sorbate, and the common specification's own warnings regarding the use of parabens with certain sweeteners, that the named inventors did not have within their possession at the time of the filing date of the '587 application the full scope of the claims of the '023 patent. There is very little stability data for 12 months or longer in the common specification, and from the forgoing information I have identified, a POSA would reasonably believe that many of the liquids falling within the formulation elements of the '023 patent claims would likely not meet the claimed stability requirements (and would therefore be inoperable). There is simply no support for Azurity's claim that the tens (likely hundreds) of thousands of enalapril liquids covered by the formulation elements of the '023 patent claims would actually meet the stability requirements of those claims, and based on the information contained in the common specification and the POSA's knowledge, the POSA would not believe that to be the case.

86. All of the claims of the '023 patent either permit (claims 1-12, 14-18, 20) or require (claims 13 and 19) a paraben preservative. However, there is absolutely no description in the common specification of such liquids actually being stable for 12 months or longer, nor is there

anything in the common specification suggesting that such liquids would actually meet the stability requirements of those claims. In fact, as I've explained above, to the contrary—from at least the Example C data in the common specification, the POSA would expect that paraben preserved liquids falling within the scope of these claims would be inoperable and would not meet the stability requirements of the claims

87. Finally, it is worth noting that during prosecution of the First Wave Patents, Azurity argued that the 12-month stability shown for the narrow formulations claimed in those patents (with specific concentrations of enalapril, citric acid, sodium citrate, and sodium benzoate), were unexpected, and that:

> **As such, the prior art does not provide any expectation that any <u>particular</u> combination would be successful for stable enalapril oral liquid formulations, much less any expectation that the combination of [sic] with enalapril, citric acid, sodium citrate, sodium benzoate, sucralose and water at the recited concentrations and at a pH of less than about 3.5 would be successful in forming a stable enalapril liquid formulation.**

Ex. H, Prosecution History of U.S. Patent Appl. No. 15/081,603 ("'603 PH"), Feb. 3, 2017 Amendment in Resp. to Non-Final Office Action Dated Jan. 17, 2017 at 18-22 (SLVGT-EPA_0000874-878) (emphasis in original); Ex. A, D. Del. 18-1962 ECF No. 195, Trial Tr. Vol. B, Moreton 397:25-398:25. Azurity argued that the 12-month stability demonstrated under refrigerated conditions "could not have been predicted or contemplated." Ex. H, '603 PH, Feb. 3, 2017 Amendment in Resp. to Non-Final Office Action Dated Jan. 17, 2017 at 22 (SLVGT-EPA_0000878). Azurity made essentially these same unexpected results arguments during prosecution of the '587 application, which issued into the '023 patent. ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, Apr. 23, 2021 Resp. at 9 (BION-ESOL-00038477) ("The unexpected stability results of the presently claimed formulations are not taught by, and could not have been

predicted or contemplated by [the prior art].”). These arguments reinforce my opinion that a POSA would not believe from the common specification—which contains no description of enalapril liquids stable at 12 months beyond the narrow Example E liquids—that the named inventors were in possession of the claimed enalapril liquids as of the filing date of the ’587 application (January 15, 2021).

b. Formulations with No Separate Buffer Component

88. The ’023 patent is the first patent in Azurity’s enalapril liquid patent family (which includes the First Wave Patents, the Second Wave Patents, and the ’023 patent) that claims stable enalapril liquids without a buffer component. There is absolutely no support for this aspect of the ’023 patent claims in the common specification.

89. First, a POSA reading the common specification would know that all of the example formulations provided—not just the Example E formulations, which were the only ones shown to be stable for at least 12 months under refrigerated conditions—contain a separate, independent buffer component, and that buffer component is always citric acid and sodium citrate. See Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶ 211 (“The common specification simply does not describe enalapril liquid formulations using buffers beyond citric acid/sodium citrate at specific concentrations that are stable for 12 months under refrigerated conditions. That includes enalapril liquid formulations using buffers qualitatively different than citric acid/sodium citrate . . . .”). There is simply no example provided in the common specification of an enalapril liquid that does not contain a separate independent buffer component, stable or otherwise.

90. Second, a POSA reading the common specification would not believe that an enalapril liquid without a buffer component could be stable under refrigerated conditions for 12

months. The common specification explains that at a pH of above 3.5, enalapril degradation into enalaprilat increases, and that below a pH of 4 enalapril degradation into enalapril diketopiperazine increases. ECF No. 1-1, Compl. Ex. A, '023 patent 14:41-45. Moreover, a POSA reading the examples in the common specification would understand that the only formulations reported to be stable at 12 months under refrigerated conditions (the Example E liquids) had pHs between 3-3.5, and that the example formulations at higher pHs (*e.g.*, the Example A2-A6 and Example C formulations) likely were not stable at 12 months under refrigerated conditions. *Id*. at Examples A-E. And a POSA would also know that—as Azurity's expert, Dr. Byrn, admitted in connection with the First and Second Wave Suits—"pH is related to stability, and pH changes will cause [enalapril] to degrade." Ex. G, D. Del. 18-1962 ECF No. 235, Mar. 31, 2021 Byrn Decl. ¶ 18. However, without a buffer component, a POSA would also know that there would be nothing in the enalapril liquid to maintain the pH of the formulation within the 3-3.5 window for optimal stability. The common specification never addresses this concern, and never explains or even suggests that an enalapril liquid without a separate, independent buffer component could be stable for at least 12 months under refrigerated conditions.

91. In the April 23, 2021 Mosher Declaration submitted during prosecution of the '587 application—where Dr. Mosher described for the first time enalapril liquids without a separate, independent buffer component—Dr. Mosher stated that "[f]ormulations of Table 1 do not require additional buffering agents other than enalapril maleate, which is a salt of an amino acid. As an amino acid, an enalapril molecule contains carboxylic acid and amine groups that can dissociate and thus balance the pH variations." ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, Apr. 23, 2021 Mosher Decl. at 5 (BION-ESOL-00038484). But there is absolutely no support for this assertion anywhere in the common specification. There is nothing even suggesting that enalapril can

"balance pH variations." To the contrary, portions of the common specification would lead a POSA to believe that enalapril (or its pharmaceutically acceptable salt or solvate) would be insufficient by itself to balance the pH of an enalapril liquid and be "self-stable."

92. As I have pointed out, every example of an enalapril liquid in the common specification contains enalapril maleate and a separate, independent "buffering agent." The common specification defines "buffering agents" as those agents that "maintain the pH of the liquid enalapril formulation." ECF No. 1-1, Compl. Ex. A, '023 patent 13:35-36. The common specification goes on to identify at least 38 different buffering agents—enalapril and its pharmaceutically acceptable salts/solvates are not identified on that list. *Id*. at 13:36-57. The entire "Summary of the Invention" section of the common specification describes only enalapril liquids with separate independent citrate buffers. *Id*. at 2:29-4:61.

93. As Dr. Byrn opined in connection with the First and Second Wave Suits, enalapril "is known to have stability issues once dissolved into a solution. . . . Thus, a liquid formulation of enalapril would generally be expected to have a short shelf-life (e.g., on the order of weeks to only a few months)." Ex. G, D. Del. 18-1962 ECF No. Mar. 31, 2021 Byrn Decl. ¶ 5. The common specification suggests that a way around these stability problems is the inclusion of a separate, independent citrate buffer component that maintains pH of the enalapril liquid between 3-3.5. But now, in the '023 patent, Azurity has claimed what no POSA would reasonably believe Azurity had possession of when it filed for the '023 patent—enalapril liquids without a separate, independent buffer component that are stable under refrigerated conditions for at least 12 months. There is simply nothing in the common specification suggesting that enalapril liquids without separate, independent buffer components could be stable for at least 12 months under refrigerated conditions, and the claims of the '023 patent are invalid for this additional reason.

c. Buffered Formulations where the Buffer Is Not a Citrate Buffer

94. As I have explained above, the claims of the ’023 patent cover enalapril liquids that may include a separate, independent buffer component (even though the claims themselves do not expressly require a separate buffer component). And the common specification identifies at least 38 different buffering agents as suitable for use in the claimed liquids. ECF No. 1-1, Compl. Ex. A, ’023 patent 13:35-57. However, as I have explained at paragraphs 210-211 of my April 19, 2021 Declaration, which I incorporate herein by reference, the common specification simply does not describe enalapril liquids that are stable for 12 months under refrigerated conditions using buffers beyond citric acid/sodium citrate at specific concentrations. Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶¶ 210-11. That includes enalapril liquids using buffers qualitatively different than citric acid/sodium citrate—there is not one single enalapril liquid described in the common specification that is stable for 12 months under refrigerated conditions that uses a phosphate buffer, a citrate/phosphate buffer, an acetate buffer, a glycine buffer, or a tartrate buffer, or any other buffer beyond a citrate buffer at specific concentrations (those described in Example E), and a POSA would simply not believe that the named inventors had possession of any such liquid as of the filing date of the ’587 application based on the common specification. For this additional reason, the claims of the ’023 patent lack written description support.

d. Buffers that Have No pKa within ± 1 of the Formulation pH

95. As I explained in my First Wave Rebuttal Report, a buffer maintains the pH of an aqueous liquid, and is usually comprised of a weak acid and its conjugate base. Ex. C, 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. Ex. A, First Wave Rebuttal Report ¶¶ 95-116. The

formulation elements of the '023 patent claims literally cover enalapril liquids that use non-functional buffers.

96. The main purpose of a buffer is to maintain formulation pH, something critically important with respect to enalapril liquids as the POSA would know from both the common specification and from the prior art that the optimal pH for enalapril stability in water is between 3-3.5. *See* ECF No. 1-1, Compl. Ex. A, '023 patent 14:9-45; *id*. at Examples A-E; Ex. I, Ip and Brenner, 16 ANALYTICAL PROFILES OF DRUG SUBSTANCES 207, 236 (1987) (DTX2048.30) ("Ip and Brenner"); ECF No. 9-7, Shrestha Decl. Ex. G, Op. at 28. However, as I have explained in my April 19, 2021 Declaration, and as the Delaware court found at trial in the First Wave Suits, a POSA would know that for a buffer to adequately maintain pH (i.e., for a buffer to be functional), the strength of the weak acid component (or the weak acid's pKa) must be within ± 1 of the formulation pH. Ex. C, D. Del. 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶ 75; ECF No. 9-7, Shrestha Decl. Ex. G, Op. at 13-14; Ex. J, Daniel C. Harris, EXPLORING CHEMICAL ANALYSIS, 189-253, 198 (5th ed. 2013) (DTX-1087.12); Ex. K, Glasstone, S. and Lewis, D., ELEMENTS OF PHYSICAL CHEMISTRY 545-47 (MacMillan & Co., 2nd ed. 1960) ("Glasstone") (DTX-1086.4); Ex. B, 18-1962 ECF No. 196, Sealed Trial Tr. Vol. B, Moreton 521:22-522:9, 523:18-524:12.

97. The claims of the '023 patent, much as the claims of the '868 and '621 patents, cover enalapril liquids that use non-functional buffers, i.e., buffers that do not have an acidic hydrogen with a pKa within ± 1 of the formulation pH—but such formulations are nowhere described in the common specification, let alone as stable for 12 months under refrigerated conditions. For instance, in the First and Second Wave Suits, Azurity took the position that maleic acid dissociated from enalapril maleate reacts with sodium hydroxide added during the penultimate

step of Bionpharma's formulation process to form *in situ* a maleic acid/sodium maleate buffer. However, the pKa of the first acidic hydrogen on maleic acid is 1.97, while the second acidic hydrogen on maleic acid has a pKa of 6.24. Ex. B, 18-1962 ECF No. 196, Sealed Trial Tr. Vol. B, Byrn 432:5-7; *id*. at Moreton 539:4-14. The formulation pH range of Bionpharma's ANDA product and Epaned® is about 3-35, and maleic acid has no acidic hydrogen within ± 1 of this formulation pH range.

98. As another example, the common specification identifies sodium acetate as a suitable buffer for use in the claimed liquids. ECF No. 1-1, Compl. Ex. A, '023 patent 13:45. The pKa of the acidic hydrogen on acetic acid (the conjugate acid of sodium acetate) is 4.76. Ex. E, HPE at 5 (acetic acid entry). But if the formulation pH is about 3 (the optimal pH for enalapril stability), an acetate buffer would not be functional, yet the formulation elements of the '023 patent claims would literally cover an enalapril liquid formulation using an acetate buffer at a pH of about 3 (assuming all the other formulation elements are met).

99. Simply put, the common specification does not describe any enalapril liquids that have non-functional buffers (buffers with weak acid components that only have pKa's outside of ± 1 of the formulation pH), let alone such formulations that are stable under refrigerated conditions for at least 12 months, even though such formulations would literally meet the formulation elements of the claims of the '023 patent. A POSA would simply not believe that the named inventors had within their possession as of the filing date of the '587 application enalapril liquids that use non-functional buffers and that are stable for at least 12 months under refrigerated conditions. For this additional reason, the '023 patent claims lack written description support.

e. Formulations with pH beyond 3-3.5

100. As I have explained above, the common specification discloses that the pH range for optimal stability of enalapril in the disclosed liquids is 3-3.5. ECF No. 1-1, Compl. Ex. A, '023 patent 14:41-45; *id*. at Examples A-E. A POSA reading the examples in the common specification would understand that the only formulations reported to be stable at 12 months under refrigerated conditions (the Example E liquids) had pHs between 3-3.5, and that the example formulations at higher pHs (e.g., the Example A2-A6 and Example C formulations) likely were not stable for 12 months under refrigerated conditions. ECF No. 1-1, Compl. Ex. A, '023 patent at Examples A-E.

101. Further, as evidenced by numerous literature references, the POSA would know that enalapril had maximum stability at a pH of approximately 3. Ex. I, Ip and Brenner at 236 (DTX2048.30); Ex. L, Allen, L. at al., *Stability of alpraxolam, chloroquine phosphate, cisapride, enalapril maleate, and hydralazine hydrochloride in extemporaneously compounded oral liquids*, 55 AM J. HEALTH-SYST PHARM 1915, 1917 (1998) (DTX-2056.3); Ex. M, Sosnowska, K. et al., *Stability of Extemporaneous Enalapril Maleate Suspensions for Pediatric Use Prepared From Commercially Available Tablets*, 66 ACTA POLONIAE PHARMACEUTICA - DRUG RES. (3) 321, 322 (2009) (DTX-2055.2). Thus, the POSA reading the common specification would already understand from literature going back to the late 1980s that enalapril degradation in aqueous formulations was greatly influenced by pH, and that a pH of approximately 3 was required for maximum stability. Azurity's expert in the First and Second Wave Suits, Dr. Byrn, even confirmed in a declaration that "pH is related to stability, and pH changes will cause the drug to degrade." Ex. G, 18-1962 ECF No. 235, Mar. 31, 2021 Byrn Decl. ¶ 18.

102. While Azurity's expert in the instant suit, Dr. Buckton, asserts that the POSA "would understand that the specification instructs that modulation of the pH provides a lower

impurity profile" (ECF No. 25-6, Buckton Decl. ¶ 23), I note that claims 1-3 and 6-20 of the '023 patent have no restriction on pH whatsoever, and thus include within the literal scope of the formulation elements of those claims enalapril liquids with pHs beyond 3-3.5. It is my opinion that a POSA would not reasonably believe that the named inventors had within their possession at the time of the filing date of the '587 application the full scope of the formulations covered by claims 1-3 and 6-20 of the '023 patent, because the POSA would understand from their own knowledge and from the common specification that enalapril liquid formulations with pHs outside of 3-3.5 would likely not meet the stability requirements of the claims.

f. Formulations stable for 18-24 months

103. Claims 2 and 3 depend from claim 1 and specify that the formulation of claim 1 is stable under refrigerated conditions for at least 18 months and at least 24 months, respectively. There is absolutely no description in the common specification of any enalapril liquid that is stable for 18 months or longer. The only data provided for enalapril liquids at 12 months or longer (under any conditions) is for the Example E formulations: the data for the E1, E2, E3, and E4 liquids under refrigerated conditions goes out to 62 weeks, which is about 14.5 months. ECF No. 1-1, Compl. Ex. A, '023 patent at Examples A-E.

104. As explained at paragraph 158 of my April 19, 2021 Declaration (Ex. C hereto), which I incorporate herein by reference, Azurity argued during prosecution of the First Wave Patents that the stability exhibited by the narrow group of enalapril liquids claimed therein was unexpected, and Azurity made the same unexpected results arguments for formulations claimed in the Second Wave Patent. *E.g.*, Ex. G, '603 PH, Feb. 3, 2017 Amendment in Resp. to Non-Final Office Action Dated Jan. 17, 2017 at 22 (SLVGT-EPA_0000878)

105. Azurity also made the same unexpected results arguments during prosecution of the '587 application, describing the stability exhibited by liquids of the '023 patent claims as something that "could not have been predicted or contemplated." ECF No. 9-22, Shrestha Decl. Ex. V, '587 PH, Apr. 23, 2021 Resp. at 9 (BION-ESOP-00038477). Those arguments were for 12 month stability (more accurately, as I explain further below, for 12 week stability that Dr. Mosher improperly extrapolated out to 12 months); Azurity never came forward, either in the common specification or in the April 23, 2021 Mosher Declaration, with any evidence that the liquids claimed in any of the '023 patent claims could be stable for 18 months or longer.

106. Because there is simply no description in the common specification of any enalapril liquid that is stable for 18 months or longer under refrigerated conditions, and because—as Azurity conceded during prosecution—enalapril liquid stability is unpredictable and any stability Azurity was able to demonstrate for the Example E formulations and for those in the April 23, 2021 Mosher Declaration was unexpected, a POSA would simply not believe that the named inventors had within their possession at the time Azurity filed the '587 application enalapril liquids that are stable for 18 months or longer. Therefore, claims 2-3 lack written description support.

g. Paraben Preserved Formulations

107. The claims of the '023 patent either require (claims 13 and 19) or may contain (claims 1-12, 14-18, 20) a paraben preservative. ECF No. 1-1, Compl. Ex. A, '023 patent at claims. There is absolutely no description in the common specification of any paraben preserved enalapril liquids that are stable under refrigerated conditions for 12 months or longer. In fact, as I have explained above, the specification would lead the POSA to the conclusion that paraben preserved enalapril liquids falling within the formulations elements of the '023 patent claims would likely not meet the stability requirements of those claims. *See, e.g.*, ECF No. 1-1, Compl. Ex. A, '023

patent at Example C; Ex. B, 18-1962 ECF No. 196, Sealed Trial Tr. Vol. B, Byrn 428:24-429:6 (Dr. Byrn testifying that the Example C paraben preserved formulations were inoperable); Ex. D, 18-1962 ECF No. 194, Sealed Trial Tr. Vol. A, Byrn 296:19-298:9 (same). For these reasons, it is my opinion that a POSA would not believe that the named inventors had within their possession as of the filing date of the '587 application paraben preserved formulations falling within the scope of all claims of the '023 patent, and that those claims therefore lack written description support.

h. Formulations with Sodium Benzoate Concentration Beyond "about 1 mg/ml"

108. As I explained in my April 19, 2021 Declaration (Ex. C hereto) at paragraphs 161-165, which I incorporate by reference as if fully set forth herein, during prosecution of the Second Wave Patents, the PTO Examiner rejected Azurity's attempt to claim stable enalapril liquids preserved with sodium benzoate beyond a concentration of "about 1 mg/ml." That is because—and I believe the Examiner got this correct—the only enalapril liquids described in the common specification as being stable for about 12 months or longer were preserved with 1 mg/mL of sodium benzoate (the Example E liquids). *See* ECF No. 1-1, Compl. Ex. A, '023 patent at Examples A-E.

109. Because, as the Examiner agreed during prosecution of the Second Wave Patents, enalapril liquids preserved with sodium benzoate at concentrations beyond "about 1 mg/ml" and stable for at least 12 months under refrigerated conditions have absolutely no support in the common specification, it is my opinion that all of the '023 patent claims (which each permit inclusion of sodium benzoate at a concentration beyond 1 mg/mL) lack written description support for this additional reason.

i. Formulations with Buffer Concentrations Beyond 5-10 mM

110. As I have explained herein, by its literal scope, each of the claims of the '023 patent permits the inclusion of a buffer component, which is not restricted by concentration. As I have discussed herein, the only enalapril liquids described as stable for at least 12 months under refrigerated conditions are the Example E liquids. I have calculated the molar concentration of the buffer component of each of the Example E liquids as follows:

	E1	**E2**	**E3**	**E4**	**E5**	**E6**
Citric acid (mg/mL)	3.29	3.29	3.29	3.29	1.65	0.82
Sodium citrate (mg/mL	0.75	0.75	0.75	0.75	0.38	0.19
Citrate molar concentration (mM)	20	20	20	20	10	5

111. As can be seen, the only enalapril liquids described in the common specification as being stable for at least 12 months under refrigerated conditions have a citrate buffer molar concentration between 5-20 mM. Thus, although the literal scope of the '023 patent claims reaches enalapril liquids containing buffers at molar concentration beyond 5-20 mM, there is no support for such liquids in the common specification as being stable for 12 months or longer under refrigerated conditions, and a POSA would not believe that Azurity possessed such formulations at the time it filed for the '023 patent, given the unpredictable nature of enalapril liquid stability.

j. Formulations Containing Sugars and/or Sugar Alcohols

112. As I have explained above, the claims of the '023 patent either require (claims 13 and 19) or may contain (claims 1-12, 14-18, 20) a paraben preservative. ECF No. 1-1, Compl. Ex. A, '023 patent at claims. However, as I have also explained, the common specification expressly teaches that paraben preservatives can be incompatible with many sugars and sugar alcohols because of transesterification reactions that create additional degradants. And, in my opinion,

there is absolutely no description of any enalapril liquid in the common specification of a paraben preserved enalapril liquid formulation that contains a sugar or sugar alcohol and is stable under refrigerated conditions for at least 12 months, despite the fact that such a liquid can fall squarely within the formulation elements of the ’023 patent claims. There are simply no “blaze marks” in the common specification suggesting that paraben preserved enalapril liquid formulations that contain sugars or sugar alcohols can be stable for at least 12 months.

113. Because of this, it is my opinion that a POSA would not believe that the named inventors had within their possession as of the filing date of the ’587 application the full scope of the enalapril liquids covered by the ’023 patent claims, and those claims are invalid for lack of written description.

2. The ’023 Patent Claims Are Not Enabled and Are Therefore Invalid

a. The POSA Would Understand that the ’023 Patent Claims Cover Numerous Inoperable Embodiments

114. As I explained above, the claims of the ’023 patent—much like the claims of the ’868 and ’621 Second Wave Patents—are of enormous breadth, as the formulation elements cover tens (possibly hundreds) of thousands of enalapril liquids. A POSA would simply not believe that all, or even many, of those liquids would meet the stability limitations of the ’023 patent claims. This is because each claim covers enalapril liquids that the common specification indicates will likely not be stable under refrigerated conditions for at least 12 months. For instance, as I have explained above, claims 1-3 and 6-20 of the ’023 patent have no restriction on pH; however, a POSA would know from the POSA’s own knowledge and from the teachings in the common specification that enalapril’s maximum stability is at a formulation pH of approximately 3, and that at a pH above 3.5 enalaprilat formation is increased, while at a pH of below 4, enalapril

diketopiperazine formation is increased. *See also* Ex. G, 18-1962 ECF No. 235, Mar. 31, 2021 Byrn Decl. ¶ 18 ("pH is related to stability, and pH changes will cause [enalapril] to degrade.").

115. Similarly, as I have explained, above, the claims of the '023 patent either require or permit paraben preservatives; however, a POSA would understand from the data presented in Example C that paraben preserved formulations, particularly at a pH over 3.5, would likely not meet the stability requirements of the '023 patent claims. Furthermore, the '023 patent claims all require the presence of a sweetener. ECF No. 1-1, Compl. Ex. A, '023 patent at claims. For at least '023 patent claims 1-5 and 10-18, that sweetener could be a sugar or sugar alcohol. *Id*. at 8:44-9:16 and at claims. However, a POSA would not believe that paraben-preserved liquids falling within the scope of the formulation elements of the '023 patent claims that contain a sugar and/or sugar alcohol would meet the stability requirements of the '023 patent claims because of the express warning of incompatibility contained in the common specification. *Id*. at 13:18-31.

116. As Azurity's expert in the First and Second Wave Suits, Dr. Byrn, explained, enalapril was "known to have stability issues once dissolved into a solution," and that "a liquid formulation of enalapril would generally be expected to have a short shelf-life (e.g., on the order of weeks to only a few months)." Ex. G, 18-1962 ECF No. 235, Mar. 31, 2021 Byrn Decl. ¶ 15. Based on at least the foregoing, it is my opinion that a POSA would reasonably believe that each of the claims of the '023 patent covers numerous inoperable embodiments. Indeed, Dr. Byrn testified at trial in the First Wave Suits that the Example C paraben formulations—each of which meets the formulation elements of at least several claims of the '023 patent—were inoperable based on the data presented in Example C. Ex. B, 18-1962 ECF No. 196, Sealed Trial Tr. Vol. B, Byrn 428:24-429:6; Ex. D, 18-1962 ECF No. 194, Sealed Trial Tr. Vol. A, Byrn 296:19-298:9.

b. Undue Experimentation Would Be Required to Practice the Full Scope of the '023 Patent Claims

117. In my opinion, it would be nearly impossible for a POSA to practice the full scope of the claims of the '023 patent, mainly because of their sheer breadth and the inordinate (and undue) amount of experimentation that would be required to determine which liquids falling within the scope of the formulation elements of the claims would actually be operable (i.e., would also meet the stability requirements of the claims). Below, I apply the *Wands* factors that I understand the Court looks to in determining whether undue experimentation is required to practice the full scope of a patent claim.

i. Quantity of Experimentation Necessary

118. As I have explained above at paragraphs 75-77, the formulations elements of each of the claims of the '023 patent cover tens (and, likely, hundreds) of thousands of enalapril liquids. Focusing on just claim 1 (the sole independent claim), to practice the full scope and find out which embodiments are operable or not, the POSA would need to prepare tens (likely hundreds) of thousands of enalapril liquids—each containing the required components at varying concentrations, with some including additional components, such as a buffer (at varying concentrations)—and put those all on long-term (12 month) stability testing (in the case of '023 patent claims 2 and 3, for up to 18 and 24 months, respectively), and then analyze those results to see which of the tens (likely hundreds) of thousands of liquids would meet the stability requirements of claim 1. This task would be next to impossible, if not impossible, because of the sheer number of enalapril liquids covered by the formulation elements of claim 1. To say that undue experimentation would be required to practice the full scope of the claims is an understatement, in my opinion.

ii. Is the Experimentation Routine

119. While preparing a few dozen or even a few hundred enalapril liquids might be routine work for a POSA, preparing thousands of liquids, placing all of those on stability studies for a year or longer, and analyzing the results would be a herculean task. Of course, as explained above, the formulation elements of each claim of the ’023 patent cover more than a few thousand enalapril liquids. Preparing all of the tens (if not hundreds) of thousands of enalapril liquids meeting the formulation elements of each claim (at varying concentrations and pHs), and placing those on long-term stability studies and then analyzing those results would be anything but routine—it would be unheard of in the scientific world.

iii. Does the Patent Disclose Specific Working Examples?

120. As explained above, during prosecution, Azurity pointed to the Example E formulations as written description support for the claims of the ’023 patent. ECF No. 9-22, Shrestha Decl. Ex. V, ’587 PH, Apr. 23, 2021 Resp. at 6 (BION-ESOL-00038474). As I have also explained above, the six Example E liquids are very similar, with each containing 1 mg/mL of enalapril maleate, a citric acid and sodium citrate buffer system at specific concentrations, and 1 mg/mL of sodium benzoate as a preservative, and having a pH of approximately 3.3. Of course, the claims of the ’023 patent are much broader than the Example E formulations, and the Example E formulations are simply not commensurate in scope with the enormous breadth of the ’023 patent claims. For instance, the claims of the ’023 patent cover stable enalapril liquids that use paraben preservatives, and also liquids that have no separate buffer component; such liquids are not supported by the Example E liquids, and, in fact, have no support in the common specification whatsoever.

121. As I’ve explained extensively herein, there are no working examples provided for paraben preserved enalapril liquids that are stable for 12 months under refrigerated conditions, and

thus nothing supporting the '023 patent claims, which either require or permit paraben preservatives. As I've also explained herein, certain working examples would lead a POSA to believe that many of the enalapril liquids falling within the formulation elements of the '023 patent claims would not meet the claimed stability requirements (*e.g.*, Example C formulations).

122. Thus, not only is there a dearth of working examples in the common specification, the working examples disclosed in the common specification provide the POSA with very little guidance, if any, as to which of the tens (likely hundreds) of thousands of enalapril liquids meeting the formulations elements of the '023 patent claims would meet the stability requirements of the claims.

iv. Amount of Guidance Presented in the Patent

123. As I've explained in the previous paragraphs, the common specification provides little guidance for a POSA looking to determine which of the tens (likely hundreds) of thousands of enalapril liquids covered by the formulation elements of each claim of the '023 patent would also meet the stability requirements of the claim. The specification does advise as to optimum pH for stability, as I have explained above in Paragraphs 90, 100-101, and on incompatibility of parabens with certain sugars and sugar alcohols, as I have explained throughout herein. Beyond that, however, there is no guidance in the common specification as to which of the tens (likely hundreds) of thousands of enalapril liquids meeting the formulation elements of each claim would meet the stability requirements of the claim. In fact, certain disclosures in the common specification—such as the Example C liquids and the data provided for those liquids, which strongly suggest that those liquids would not meet the stability requirements of the claims, even though each of the Example C liquids would meet the formulation elements of at least several of the '023 patent claims—would confuse the POSA. Thus, in my opinion, all things considered, the

common specification provides a POSA with very little guidance to practice the full scope of the '023 patent claims.

v. The Nature and Predictability of the Field

124. I agree with Azurity's repeated statements during prosecution of the First and Second Wave Patents and the '023 patent that enalapril liquid stability is generally an unpredictable endeavor. Ex. C, 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. ¶¶ 15-41, 180. Azurity even emphasized in its opening statement at trial in the First Wave Suits the unpredictability of enalapril liquid stability. Ex. N, 18-1962 ECF No. 193, Trial Tr. Vol. A, 52:25-53:7 (Azurity's Opening Statement: "Another problem Amneal has is the unpredictability in the art. . . . [C]ould a [POSA] predict the ingredients needed to achieve a liquid form of enalapril . . . that would be stable for the required 24-month shelf life? The answer is no."). And Azurity's expert in the First and Second Wave Suits, Dr. Byrn, declared that enalapril "is known to have stability issues once dissolved into a solution," and that "a liquid formulation of enalapril would generally be expected to have a short shelf-life (e.g., on the order of weeks to only a few months)." Ex. G, 18-1962 ECF No. 235, Mar. 31, 2021 Byrn Decl. ¶ 15.

125. Moreover, as I explained in my April 19, 2021 Declaration at paragraphs 185-204, which I incorporate as if fully set forth herein, while a POSA would have confidence using routine experimentation and optimization that a stable enalapril oral liquid could be developed from prior art formulations such as the Epaned® Kit formulation, this does not mean that a POSA could predict which enalapril liquids would be stable and which would not—as one of Azurity's experts, Dr. Buckton, testified during trial in the First Wave Suits, there really is no substitute for long-term stability studies. Ex. O, 18-1962 ECF No. 199, Trial Tr. Vol. D., Buckton 856:12-20 ("And it says you should continue to test for a period of time sufficient to cover shelf life. So the reason for this statement is that you need 12-months long-term stability data to have confidence in how

the product is going to behave. The reason for that is if you have, say, three months' data and with no degradation, then that doesn't mean you have no degradation over 12 months. You can't make that extrapolation.").

vi. Level of Ordinary Skill in the Art

126. As set forth in Paragraph 34, *supra*, I provided my opinion on the level of ordinary skill in the art in connection with my First Wave Rebuttal Report (Ex. A to Ex. C hereto), and I incorporate that opinion as if fully set forth herein.

vii. The Scope of the Claimed Invention

127. As I explained in connection with the first *Wands* factor, and throughout my opinions herein with respect to the '023 patent, the claims of the '023 patent are of enormous breadth, and the level of disclosure in the common specification is simply nowhere near commensurate with the breadth of the claims. The common specification provides almost no guidance for a POSA to determine which of the tens (likely hundreds) of thousands of enalapril liquids meeting the formulation elements of each claim would also meet that claim's stability requirements, and it would be next to impossible for a POSA to try to figure it out herself because of the sheer breadth of the claims.

128. For the foregoing reasons, it is my opinion that the claims of the '023 patent are invalid for lack of enablement

3. Claims 1-16 and 19 of the '023 Patent Claims Are Obvious

129. If the Court does not find the '023 patent claims invalid for lack of written description or for non-enablement, it is my opinion that at least claims 1-16 and 19 of the '023 patent, which each include within their scope enalapril liquids where the only preservative is a paraben or mixture of parabens, are invalid as obvious in view of the prior art for the same reasons

expressed in paragraphs 185-204 and 262-267 of my April 19, 2021 Declaration, which I incorporate herein by reference. The prior art I rely upon for my obviousness opinions for '023 patent claims 1-16 and 19 are attached hereto as follows: Ex. I, Ip and Brenner; Ex. E, HPE; Ex. P, U.S. Food and Drug Administration, *Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances and Products* (Nov. 2003, Rev. 2) ("FDA Stability Guidance"); and Ex. Q, U.S. Patent No. 8,568,747 B1 ("'747 patent").

130. Dr. Buckton's criticisms of Ip and Brenner are misplaced. See ECF No. 25-6, Buckton Decl. ¶ 18. The POSA would not need to rely on Ip and Brenner for "formulation assistance as to how to embark on developing a stable solution formulation" beyond Ip an Brenner's teaching that enalapril has optimal stability in aqueous formulations at a pH of 3—that teaching indisputably conveys to a POSA that enalapril maleate was more stable at a pH of around 3 than at higher pHs, and a POSA would thus know to target a pH of around 3 to maximize enalapril stability in aqueous formulations.

131. I understand that, as it did during prosecution of the '023 patent, Azurity and its experts may point to the April 23, 2021 Mosher Declaration as evidence of that the claimed formulations achieve "unexpected" stability. I respectfully disagree that the April 23, 2021 Mosher Declaration serves as evidence that the claimed formulations would be stable for at least 12 months under refrigerated conditions (or at any conditions). Dr. Mosher's April 23, 2021 Declaration only provides 12-week data for the "exemplary formulations" (V-3.0, V-3.3, V3.5, X-1 and X2), not 12-month data. Dr. Mosher tries to get around this by extrapolating the 12-week data out to 12 months, but this is scientifically improper for the reasons I explained at paragraph 146 of my April 19, 2021 Declaration, which I hereby incorporate by reference as if fully set forth herein. As I explained therein, FDA Guidance generally permits extrapolation for only one and a

half times the experimental data available. Ex. C, 18-1962 ECF No.247, Apr. 19, 2021 Moreton Decl. ¶ 146 n.5. Thus, under FDA Guidance rules, at best for Azurity, the 12-week data in Dr. Mosher's April 23, 2021 Declaration could be extrapolated out to 30 weeks, which is considerably shorter than 12 months. For this reason, it is my opinion that nothing in the April 23, 2021 Mosher Declaration demonstrates "unexpected results" or even that the claimed formulations could be stable for at least 12-months under refrigerated conditions.

F. Bionpharma's ANDA and ANDA Product Do Not Infringe '023 Patent Claims 17-18 and 20.

132. Claims 17, 18, and 20 of the '023 patent require the presence of sodium benzoate. Bionpharma's ANDA product does not contain sodium benzoate. It is also my opinion that methylparaben and propylparaben are not equivalent to sodium benzoate, as I explained in detail at trial in the First Wave Suits and in my First Wave Rebuttal Report—I hereby incorporate those opinions as if fully set forth herein. *See* Ex. B, 18-1962 D.I. 196, Sealed Trial Tr. Vol. B, Moreton 554:13-565:9; Ex. C, 18-1962 ECF No. 247, Apr. 19, 2021 Moreton Decl. Ex. A, First Wave Rebuttal Report ¶¶ 211-223.

133. Moreover, for any assertion from Azurity that the methylparaben and propylparaben in Bionpharma's ANDA product can meet the sodium benzoate limitation of '023 patent claims 17, 18, and 20 equivalently, it is my opinion that such an assertion, if adopted, would vitiate the sodium benzoate limitation of these claims. This is so because claims 17, 18, and 20 may include, additionally, paraben preservatives (in addition to the claimed sodium benzoate), as claims 17 and 20 use the "comprises" transitional phraseology, which I understand is open ended (meaning that other preservatives can be included in the claimed liquids).

134. I have been advised by Bionpharma's counsel that the doctrine of equivalents cannot extend to cover the prior art, including obvious subject matter. If the Court were to find

methylparaben and propylparaben equivalent to sodium benzoate, then it is my opinion that claims 17, 18, and 20 of the '023 patent would ensnare the prior art, as they would cover an obvious version of the prior art Epaned® Kit (reconstituted) that I have relied on as the basis of my obviousness opinions (*see* paragraphs 129-130, *supra*).

XI. SUPPLEMENTAL OPINIONS

135. I reserve the right to respond to any issues raised in any declarations Azurity serves in response to this this declaration.

136. If called to testify, my testimony may include an explanation of the scientific principles that underlie the opinions expressed herein.

137. I have based my opinion and analysis on documents and information available to me at the time I signed this declaration. If and when any new evidence arises, I reserve the right to supplement or modify my opinions to reflect that evidence.

138. I reserve the right to make and use demonstratives to help explain my opinions.

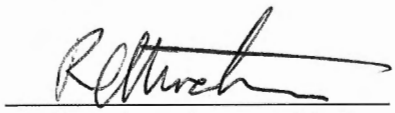
XII. COMPENSATION

139. I am being compensated for my work in this case at a rate of $600 per hour. My compensation is not dependent on the outcome of this litigation.

XIII. PRIOR TESTIMONY

140. Attached as Exhibit R is a list of actions I have provided testimony in as an expert at deposition or trial.

I hereby declare under penalty of perjury under the laws of the United States that the foregoing statements are true and correct and this declaration was executed by me on this 20th day of August, 2021.



R. Christian Moreton, Ph.D.